In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 19, 2022

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TAMARA CHAVEZ, Parent of T.C., a minor,	*	No. 16-1479V
Petitioner,	*	Special Master Nora Beth Dorsey
v.	*	Entitlement; Diphtheria-Tetanus-Acellular-Pertussis ("DTaP") Vaccine; Hepatitis B Vaccine; Inactivated Polio ("IPV") Vaccine; Haemophilus Influenzae Type B ("Hib") Vaccine; Rotavirus Vaccine; Early Infantile Epilepsy; Encephalopathy; Intractable Seizures; Gastroesophageal Reflux; Global Developmental Delay; Neurological Movement Disorder.
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	
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Patricia Finn, Patricia Finn, P.C., Nanuet, NY, for petitioner.
Andrew Henning, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

I. INTRODUCTION

On November 9, 2016, Tamara Chavez ("petitioner"), on behalf of her minor child, T.C., filed a petition under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).[2] Petitioner alleged as a result of the Pediarix (diphtheria-tetanus-acellular pertussis ("DTaP"), hepatitis B, and inactivated polio ("IPV")),

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2012). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

pneumococcal conjugate, haemophilus influenzae type B ("Hib"), and rotavirus vaccinations administered on November 13, 2013, T.C. developed "Early Infantile Epilepsy resulting in Encephalopathy, Intractable Seizures, Gastroesophageal Reflux, Global Developmental Delay[,] and Neurological Movement Disorder." Amended ("Am.") Petition at 1 (ECF No. 20). Respondent argued against compensation, stating that "this case is not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 2 (ECF No. 12).

After carefully analyzing and weighing the evidence presented in this case in accordance with the applicable legal standards, the undersigned finds that petitioner has not provided preponderant evidence that the vaccinations T.C. received on November 13, 2013 caused her to develop "Early Infantile Epilepsy resulting in Encephalopathy, Intractable Seizures, Gastroesophageal Reflux,[3] Global Developmental Delay[,] and Neurological Movement Disorder." Thus, she has not satisfied her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005), and the petition must be dismissed.

II. PROCEDURAL HISTORY

Petitioner filed her claim on November 9, 2016 alleging the Pediarix (DTaP, hepatitis B, and IPV), pneumococcal conjugate, Hib, and rotavirus vaccinations administered on November 13, 2013, as well as the DTaP, Hib, and rotavirus vaccinations, administered on January 13, 2014, significantly aggravated T.C.'s "Early Infantile Epilepsy resulting in Encephalopathy, Intractable Seizures, Gastroesophageal Reflux, Global Developmental Delay and Neurological Movement Disorder." Petition at 1 (ECF No. 1).

Petitioner filed medical records in November and December 2016. Petitioner's Exhibits ("Pet. Exs.") 1-14. On March 10, 2017, respondent filed respondent's Rule 4(c) report recommending against compensation. Resp. Rept. at 2. Petitioner was then ordered to file an expert report by May 15, 2017. Order dated Mar. 14, 2017 (ECF No. 13). An Order to Show Cause was issued on July 17, 2017, and petitioner filed an amended petition[4] and an expert report on August 14, 2017. Order to Show Cause dated July 17, 2017 (ECF No. 19); Am. Petition; Pet. Ex. 15. Respondent filed an expert report and medical literature in January 2018, and petitioner filed a supplemental expert report on April 16, 2018. Resp. Exs. A-G; Pet. Ex. 16.

The undersigned scheduled a Rule 5 conference on June 5, 2018, but found "that she could not make a decision based on the existing record, and that a two-day entitlement hearing would be necessary." Order dated June 6, 2018 (ECF No. 39). The undersigned issued a pre-

[3] Petitioner did not focus on the alleged injury of gastroesophageal reflux and the parties' experts did not address it in their causation opinions. Thus, the evidence as to the allegation was underdeveloped. Ultimately, T.C. required a G-J tube for nourishment. To the extent that petitioner seeks compensation for this alleged injury, the undersigned denies compensation, for all of the reasons stated herein.

[4] In her amended petition, petitioner amended her claim to focus on only T.C.'s November 13, 2013 vaccinations and changed the significant aggravation claim to a causation claim.

hearing Order on July 9, 2018, setting an entitlement hearing for March 5, 2019. Pre-Hearing Order dated July 9, 2018 (ECF No. 41).

Petitioner filed medical records, an expert report, medical literature, and a pre-hearing brief from October 2018 through January 2019. Pet. Exs. 17-50; Pet. Pre-Hearing Brief ("Br."), filed Jan. 22, 2019 (ECF No. 63). Respondent filed his pre-hearing brief on February 14, 2019. Resp. Pre-Hearing Br., filed Feb. 14, 2019 (ECF No. 67).

On February 21, 2019, the undersigned held a status conference stating T.C.'s genetic testing and updated medical records should be filed prior to the entitlement hearing. Order dated Feb. 22, 2019 (ECF No. 71). Petitioner filed T.C.'s genetic records, but needed additional time to file updated records. Pet. Ex. 52; see Order dated Feb. 28, 2019 (ECF No. 74). Therefore, the undersigned canceled the entitlement hearing until petitioner filed the requested records. Order dated Mar. 1, 2019 (ECF No. 75). Petitioner filed a compact disc of records, medical records, and a statement of completion on June 28, 2019. Pet. Exs. 54-55; Statement of Completion, filed June 28, 2019 (ECF No. 84). From September 2019 to June 2020, petitioner filed additional medical records and another statement of completion. Pet. Exs. 56-65; Statement of Completion, filed Apr. 23, 2020 (ECF No. 100).

The undersigned issued a pre-hearing order on August 10, 2020 setting an entitlement hearing for April 20 and 21, 2021. Pre-Hearing Order dated Aug. 10, 2020 (ECF No. 109). Respondent filed an expert report and medical literature in September and November 2020. Resp. Exs. H-AA. On November 24, 2020, petitioner filed a responsive expert report with accompanying medical literature. Pet. Exs. 66-70, 80. Respondent filed an additional expert report and medical literature on February 12, 2021. Resp. Exs. BB-CC. The parties filed their pre-hearing submissions in February and March 2021. Joint Pre-Hearing Submission, filed Feb. 22, 2021 (ECF No. 127); Pet. Supplemental Br., filed Feb. 23, 2021 (ECF No. 128); Resp. Pre-Hearing Submission, filed Mar. 15, 2021 (ECF No. 129). Respondent filed hearing documents from his expert on April 1, 2021. Resp. Ex. DD.

On April 20 and 21, 2021, the undersigned held an entitlement hearing. Both parties failed to file complete records prior to the hearing and the undersigned ordered respondent and petitioner to file additional records. Order dated Apr. 21, 2021 (ECF No. 136). The parties filed additional records and documents from April to June 2021. Resp. Exs. EE-GG; Pet. Exs. 72-79.

On November 16, 2021, petitioner filed her post-hearing brief. Pet. Post-Hearing Br., filed Nov. 16, 2021 (ECF No. 156). Respondent filed his post-hearing brief on February 17, 2022. Resp. Post-Hearing Br., filed Feb. 17, 2022 (ECF No. 159). Petitioner filed her reply on April 4, 2022. Pet. Reply, filed Apr. 4, 2022 (ECF No. 162).

This matter is now ripe for adjudication.

III. ISSUES TO BE DECIDED

The parties do not dispute the diagnosis and stipulate that T.C. has an epileptic encephalopathy. Joint Submission at 1.

The factual issue in dispute is whether T.C.'s condition preexisted her vaccinations. Joint Submission at 1. That issue will be resolved in the context of the undersigned's analysis of causation, specifically, Althen Prong Three.

Regarding causation, the parties dispute whether T.C.'s vaccinations caused T.C.'s epileptic encephalopathy pursuant to the analysis set forth in Althen. Joint Submission at 1-2.

IV. MEDICAL TERMINOLOGY

Epileptic encephalopathy encompasses a large group of disorders, in which an infant or child typically has several types of seizures associated with developmental slowing or regression that might follow seizure onset or exacerbation. Resp. Ex. E at 1.[5] It is associated with a high probability of encephalopathic features that present or worsen after the onset of epilepsy. Resp. Ex. A at 12 (citing Resp. Ex. C).[6] Epileptic encephalopathy can present along a continuum of severity and may occur at any age. Id. The condition is most common and severe in infancy and early childhood, where global and profound cognitive impairment may occur. Id. The onset of epileptic encephalopathies may occur against a background of normal or delayed development. Resp. Ex. E at 1.

Epileptic encephalopathy embodies the notion that the epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology alone (e.g., cortical malformation), and that these can worsen over time. Resp. Ex. A at 12 (citing Resp. Ex. C). The cause of epileptic encephalopathy is unknown in the majority of cases. Resp. Ex. R at 1.[7]

V. BACKGROUND

A. Summary of Relevant Facts

1. 2013 Records

T.C. was born on September 9, 2013. Pet. Ex. 2 at 3. There were no complications with petitioner's pregnancy. Id. at 50. Additionally, no labor and delivery complications were documented.

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[5] Amy McTague et al., The Genetic Landscape of the Epileptic Encephalopathies of Infancy and Childhood, 15 Lancet Neurology 304 (2016).

[6] Anne T. Berg et al., Revised Terminology and Concepts for Organization of Seizures and Epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009, 51 Epilepsia 676 (2010).

[7] Fadi F. Hamdan et al., High Rate of Recurrent De Novo Mutations in Developmental and Epileptic Encephalopathies, 101 Am. J. Hum. Genetics 664 (2017).

On September 13, 2013, T.C. presented to Dr. Alaaeldin Moawad at Long Island Pediatrics of Brentwood, P.C. ("Long Island Pediatrics") for a newborn visit. Pet. Ex. 2 at 50. T.C. was reported as doing well. Id. Dr. Moawad noted there was a "bright spot" on T.C.'s previous sonogram and recommended petitioner follow up with a cardiac evaluation. Id. Dr. Moawad's assessment was diaper rash and "undiagnosed cardiac murmurs." Id. at 50-51. The hepatitis B vaccine was administered. Id. at 51. No adverse reaction to the vaccination was noted.

T.C. returned to Long Island Pediatrics for her one month follow up appointment with Dr. Ramon Ferrand on October 11, 2013. Pet. Ex. 2 at 48. Dr. Ferrand documented that T.C. was doing well and had normal findings after an evaluation by a cardiologist. Id.

On October 25, 2013, T.C. presented to Dr. Moawad due to a rash. Pet. Ex. 2 at 46. Dr. Moawad prescribed hydrocortisone cream and administered a second hepatitis B vaccine. Id. at 46-47. No adverse reaction to the vaccination was noted. T.C.'s neurological exam was normal. Id. at 46.

T.C. returned to Dr. Moawad for a two month well baby visit on November 13, 2013. Pet. Ex. 2 at 44. T.C. received Pediarix (DTaP, hepatitis B, IPV), pneumococcal conjugate, Hib, and rotavirus vaccinations. Id. No adverse reaction to the vaccinations was noted.

On December 14, 2013, T.C. presented to Dr. Ferrand for complaints of constipation. Pet. Ex. 2 at 39. T.C. did not have any fever, vomiting, or abdominal pain. Id. Examination revealed constipation, feeding difficulties, and exotropia.[8] Id. T.C.'s neurological exam was documented as normal.

2. 2014 Records

T.C. presented to Dr. Moawad on January 13, 2014 for a four month well baby visit. Pet. Ex. 2 at 37. Her developmental assessment was appropriate for her age. Id. She was noted as having congestion and her "eyes do not line up." Id. She was assessed with unspecified exotropia and administered DTaP, Hib, and rotavirus vaccinations. Id. at 37-38. No adverse reaction to the vaccinations was noted.

On January 20, 2014, petitioner and T.C. returned to Dr. Ferrand for the IPV vaccine. Pet. Ex. 2 at 35. Pediatric exam was normal. Id. No adverse reaction to the vaccination was noted.

T.C. presented to the Good Samaritan Hospital Medical Center ("Good Samaritan") Emergency Department ("ED") on January 26, 2014 for crying spells for two days and a temperature of 100.3 degrees. Pet. Ex. 5 at 7. Dr. Luzviminda Santangelo diagnosed T.C. with

[8] Exotropia is "strabismus in which there is permanent deviation of the visual axis of one eye away from that of the other, resulting in diplopia." Exotropia, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=17892 (last visited June 9, 2022).

nasal congestion and upper respiratory infection. Id. On examination, she was normal with a low-grade fever. Id. at 10. T.C. tested negative for influenza A and B antigens. Id. She was discharged home. Id. at 13.

On January 29, 2014, T.C. followed up with Dr. Ferrand for congestion. Pet. Ex. 2 at 33. Chief complaints were congestion, follow up from ophthalmology, and she "can't hold head upright." Id. Dr. Ferrand assessed T.C. with "other disease of nasal cavity and sinuses" and developmental coordination disorder due to not fixating on objects properly and mild head lag. Id.

On January 30, 2014, T.C. arrived at Good Samaritan ED for congestion and "loud sounds when feeding" and her "body tensed up like she couldn't breath[e] for about 1 min[ute]." Pet. Ex. 5 at 31-32. Dr. Rudolph Badleo documented T.C. "had no seizure-like activity but has been having a constant [muscle twitches] which as per mom said she was born [with]. Mom said she told her pediatrician and her pediatrician said it was normal." Id. at 33. Petitioner reported she noticed T.C. "seems to twitch more frequent than before." Id. at 45. T.C.'s twitches were also described as "shivering." Id. On examination, Dr. Badleo noted T.C. was "constantly thrashing around" and "[did] not make eye contact." Id. at 35. T.C. was admitted and the initial impression was twitching vs. seizure vs. hypertonia vs. cerebral palsy. Id. An X-ray of the chest on January 31, 2014 showed "[m]ild peribronchial thickening without focal consolidation or effusion." Id. at 44.

Dr. Meghna Shah examined T.C. on January 31, 2014. Pet. Ex. 5 at 60. Dr. Shah documented her history of upper respiratory symptoms for four days prior and an episode of "stiffening of body with staring." Id. at 61. Petitioner denied T.C.'s "eyes roll[ed] back, foaming at mouth, color change, shaking or tonic-clonic motions of extremities." Id. The episode "[l]asted ~1 minute, [T.C.] picked up by mom, then immediately relaxed and started crying." Id. Physical exam was significant for constant fidgeting and movement. Id. "Parents state [T.C. has had] intermittent 'shivering' movements since birth." Id. Dr. Shah noted T.C. had an outpatient neurology appointment scheduled due to "not holding head up." Id.

Later on January 31, 2014, T.C. was assessed with possible febrile seizure and benign myoclonic jerks. Pet. Ex. 5 at 67-68. A consultant note, documented by Dr. Sarita Duchatelier, noted that "[m]om had [] concerns about what sounds like benign myoclonic jerks (1 or 2 at a time) of mostly left shoulder that have occurred off and on since birth." Id. at 69. An electroencephalogram ("EEG") performed "was markedly abnormal, even more so during a brief myoclonic jerk, EEG perhaps suggestive of hypsarr[hythmia]."[9] Id. at 75. The EEG showed "high voltage spike and slow waves . . . with burst suppression consistent with epileptic-form activity." Id. at 81. A computed tomography ("CT") scan was ordered to rule out brain atrophy or other lesion. Id. at 75. The CT brain scan without contrast done the next day, on February 1, 2014, was normal. Id. at 80.

[9] Hypsarrhythmia is "an electroencephalographic abnormality sometimes observed in infants, with random, high-voltage slow waves and spikes that arise from multiple foci and spread to all cortical areas." Hypsarrhythmia, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=24469 (last visited June 9, 2022).

T.C. was assessed by Dr. Keith Chucheong due to seizure activity on February 1, 2014. Pet. Ex. 5 at 77. His assessment was new onset epilepsy. Id. He ordered brain magnetic resonance imaging ("MRI"). Id. On February 3, 2014, an MRI without contrast showed "[n]o evidence of acute intracranial pathology." Id. at 92-93. Dr. Duchatelier examined T.C. and noted T.C. had hypotonia with head lag, increased extra-axial fluid in the temporal lobe, and dysmorphic features. Id. at 93. A repeat MRI was suggested in three months. Id. T.C. was discharged home with instructions to continue on phenobarbital. Id.

T.C. returned to the Good Samaritan ED on February 4, 2014. Pet. Ex. 5 at 187. Registered Nurse ("RN"), Ms. Ruth Tompkins, stated T.C. "arrived crying and suddenly stop[ped] . . . . When the baby stops crying, her eyes sunset [then] move around in different directions without making eye contact. The baby will then start to cry again. Seizure-like pulsation noted in arms and legs at times." Id. T.C. had a seizure in the ED, Ativan was administered and T.C. was readmitted to the hospital. Id. at 196-200.

On February 5, 2014, Dr. Daniel Engelberg documented T.C. was having seizure-like activity. Pet. Ex. 5 at 207.

> [T.C.] noted to be rigidly flailing both arms and moving head around with left lateral deviation of eyes as well as bucking of the torso. Eyes noted to be open during seizure. Order for [A]tivan was placed but event broke on it[]s own after 3 minutes and [A]tivan was not given. Child after event was noted to be post ictal and have some drool noted at mouth. Additionally[,] eyes remained deviated to the left when lids were retracted.

Id. A few hours later, T.C. likely experienced an additional seizure and Ativan was administered. Id. at 208. An EEG was performed. Id. Dr. Chucheong reviewed the EEG and found "[general] polyspike and wave, some slowing and burst su[p]pression pattern during st[age] 2 sleep. But [n]o electrographic [seizure] noted." Id. at 209. The assessment was refractory epilepsy. Id. at 210. Dr. Chucheong recommended beginning Keppra. Id.

The next day, on February 6, T.C. was noted to have additional seizures. Pet. Ex. 5 at 219-20. A vitamin B6 trial EEG was performed and showed "significant improvements, less disorganized, fewer spikes and less discontinuous." Id. at 223. The impression was "[l]ikely pyridoxine responsive seizures." Id. Additionally, after observation, T.C. was noted to have possible gastrointestinal reflux. Id. at 236. She was placed on Zantac. Id. at 218. A nutritional consultation on February 10 raised concerns about poor nutritional intake, which was thought to relate to T.C.'s vitamin B6 deficiency seizures. Id. at 253.

On February 10, 2014, a repeat MRI without contrast revealed unremarkable findings. Pet. Ex. 5 at 255. A repeat EEG continued to show "polyspikes and slow waves but improved." Id. at 262, 265. T.C. was discharged on February 11, with the recommendation to follow up with a geneticist and neurology. Id. at 268.

T.C. followed up with Dr. Ferrand after her hospital admission for unspecified seizure disorder and "[gastroesophageal] acid reflux" on February 12, 2014. Pet. Ex. 2 at 30. T.C.'s parents were concerned about her poor appetite, but reported no fever or seizure activity since she was discharged from the hospital. Id. T.C.'s pediatric exam was otherwise normal, and Dr. Ferrand assessed her with "other forms of epilepsy and recurrent seizures, without mention of intractable epilepsy." Id. Dr. Ferrand recommended T.C. follow up with neurology and continue phenobarbital and Keppra. Id. at 30-31.

T.C. presented to the North Shore University emergency room ("ER") on February 16, 2014, for four to six seizures per day involving eye rolling and arm twitching, which each lasted about one minute. Pet. Ex. 13 at 4. She was transferred to Cohen Children's Medical Center. Id. at 6.

On March 5, 2014, T.C. presented to Dr. Moawad for a follow up from the ER for seizure disorder and gastroesophageal reflux disease ("GERD"). Pet. Ex. 2 at 27. Dr. Moawad recommended T.C. continue Zantac for esophageal reflux and follow up with a pediatric neurologist for "unspecified epilepsy." Id.

T.C. returned to Dr. Ferrand on March 20, 2014 for a well-baby visit. Pet. Ex. 2 at 24. T.C. was reported to have seizures and routine visits scheduled with neurology and cardiology. Id. T.C. had cough, congestion, and a slight fever of 100.2 degrees. Id. She could not hold her head up, or sit without support, and had "decreased tone in general." Id. Dr. Ferrand recommended ibuprofen for an acute upper respiratory infection. Id. at 25.

On April 30, 2014, T.C. was hospitalized at North Shore-Long Island Jewish Hospital due to vomiting and increased seizure activity. Pet. Ex. 6 at 59. T.C. required two doses of Ativan in the ED to control a prolonged seizure. Id. at 64. Testing revealed she was positive for rhinovirus and enterovirus. Id. at 65. On May 3, 2014, a progress note stated that T.C. had "cryptogenic infantile spasms now with tonic seizures," and a flu-like illness, with increased seizure activity. Id. at 22. An EEG revealed hypsarrhythmia. Id. at 31. Additionally, T.C. was diagnosed with dysphagia. Pet. Ex. 8 at 501. T.C. was discharged on May 8, 2014. Pet. Ex. 6 at 9.

On May 6, 2014, T.C. underwent continuous video EEG monitoring at North Shore Medical Center. Pet. Ex. 8 at 502. The EEG showed severe diffuse epileptic encephalopathy. Id. at 506. "The seizures were [] different from more typical spasms in that in between the spasms there was behavior arrest with severe attenuation in the background activity." Id.

On May 10, 2014, T.C. presented to Dr. Ferrand for congestion and cough lasting one week. Pet. Ex. 2 at 21. Dr. Ferrand noted T.C. was hospitalized the prior week for positive rhinovirus with increased congestion. Id. Dr. Ferrand assessed acute bronchiolitis, acute upper respiratory infection, and infantile spasms. Id. at 22. T.C. followed up with Dr. Ferrand on May 13, 2014 for bronchiolitis. Id. at 18. Dr. Ferrand instructed petitioner to take T.C. to the ED for oxygen and steroid treatment secondary to hypoxia. Id. at 19.

T.C. followed up with Dr. Ferrand on May 15, 2014. Pet. Ex. 2 at 16. Petitioner reported T.C.'s bronchiolitis was improved, but T.C. continued to have fevers. Id. Dr. Ferrand recommended T.C. start amoxicillin and follow up with him in a few days. Id. at 17. On May 20, 2014, T.C. presented to Dr. Ferrand with nasal congestion, diarrhea, and not sleeping well. Id. at 12. Dr. Ferrand recommended saline nasal drops and albuterol nebulizer. Id. at 13. T.C. also visited her pediatric neurologist, Dr. Marrie Sykho on May 20, 2014. Pet. Ex. 8 at 497. T.C.'s assessments were neurological movement disorder; early infantile epileptic encephalopathy, refractory; infantile spasms; and global developmental delay. Id.

T.C. underwent an evaluation with a cardiologist on May 22, 2014, due to an echocardiogram that showed "a mildly dilated root and ascending aorta." Pet. Ex. 8 at 491. An EEG was performed on May 29, 2014 showed "severe bilateral cerebral dysfunction." Id. at 485.

T.C. underwent a medical genetics assessment at Children's Medical Center of New York on June 5, 2014. Pet. Ex. 8 at 444. T.C.'s medical history indicated diagnoses for epileptic seizures, infantile spasms, GERD, and severe developmental delay. Pet. Ex. 11 at 2, 4. Family history revealed T.C.'s maternal great grandmother had a history of seizures. Id. at 3. Genetic testing revealed an interstitial deletion of "uncertain significance" in chromosome 9. Pet. Ex. 8 at 444. There was a defect in the PSAT1 gene, which "codes for phosphoserine aminotransferase. Its deficiency may result in neurological effects or schizophrenia due to low levels of serine. The deletion was found to be maternally inherited." Pet. Ex. 11 at 6. The etiology of T.C.'s neurological problems remained unknown. Id.

In June 2014, T.C.'s diagnoses included early infantile epileptic encephalopathy (refractory), global developmental delay, infantile spasms, and neurological movement disorder. Pet. Ex. 8 at 435. Throughout 2014, T.C. underwent numerous medical evaluations and tests, and was repeatedly hospitalized. See, e.g., id. at 81, 171-73, 322-26, 377, 405, 423-28, 433-35, 446-50; Pet. Ex. 11 at 2-10. Due to poor feeding and several nutrition issues, a G-tube was placed in September 2014. Pet. Ex. 14 at 27. She began to receive occupational and physical therapies. Pet. Ex. 8 at 377.

3. 2015 to Present Records

T.C. presented to the ED on January 11, 2015 for "extreme lethargy." Pet. Ex. 5 at 378. T.C.'s exam was normal, though petitioner reported T.C. had seizures every day. Id. at 381-82. T.C. was diagnosed with dehydration and discharged home. Id. at 399.

T.C. underwent an overnight video EEG on January 17-18, 2015. Pet. Ex. 8 at 126. The EEG was abnormal due to indications of electroclinical seizures, multifocal myoclonic, hypsarrhythmia, multifocal spikes, and generalized slow-spike-wave complexes. Id. at 129.

On February 26, 2015, T.C. presented to North Shore Medical Group for a consultation due to symptoms of failure to thrive and feeding problems. Pet. Ex. 8 at 47. T.C. followed up with North Shore Medical Group, Division of Medical Genetics on May 28, 2015. Pet. Ex. 11 at 6. Additional testing was recommended. Id.

Another video EEG performed from September 16 through 19, 2015 showed generalized background slowing and disorganization, multifocal spikes, and was indicative of diffuse encephalopathy. Pet. Ex. 9 at 296.

On February 1, 2016, T.C. followed up with her neurologist Dr. Sykho. Pet. Ex. 9 at 81. Dr. Sykho documented T.C.'s seizures were intractable, and she had daily twitches. Id. at 86.

T.C. received her results from a molecular genetics test done at Columbia University Medical Center on November 22, 2016. Pet. Ex. 52 at 2. The test results showed a GABRB2 abnormality of "uncertain clinical significance." Id. The results stated:

> Analysis of parental samples . . . shows that this variant is not present in either parent and is a de novo finding in this individual. . . .
>
> The P252L missense variant causes a substitution of proline by leucine at position 252 in the GABRB2 protein. This proline residue is well conserved across species. This variant is predicted to be deleterious and damaging to protein structure and/or function based on in silico analyses . . . . This variant has not been observed . . . indicating it is not a common benign variant in the populations represented in these databases. To the best of our knowledge, currently this variant has not been reported to be associated with disease.
>
> GABRB2 is a member of the GABA-A receptor gene family of ligand-gated ion channels through which GABA, the major inhibitory neurotransmitter in the mammalian brain, acts. This gene has not been associated with Mendelian disease per the OMIM database (accessed November 16, 2016). However, variants in this gene have been described as candidate variants for cerebral visual impairment . . . as well as seizures . . . .
>
> At this time, the clinical significance of variants in the GABRB2 gene remains uncertain. Additional information may become available in the future, so a periodic review of the literature is recommended.

Id. The researchers at Columbia also attached the medical article by Srivastava et al.,[10] which reported a missense mutation[11] in the β2 subunit of the $GABA_A$ receptor was a cause of genetic epilepsy and intellectual disability. Id. at 4. Srivastava et al. described the condition of a 12-year-old girl with intellectual disability and epilepsy, and who through whole exome sequencing,

[10] Siddharth Srivastava et al., A Novel Variant in GABRB2 Associated with Intellectual Disability and Epilepsy, 164A Am. J. Med. Genetics Part A 2914 (2014).

[11] A missense mutation is "a mutation that changes a codon so that it codes for a different amino acid." Missense Mutation, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=91053 (last visited June 8, 2022).

was discovered to have a de novo[12] heterozygous missense variant in exon 4 of GABRB2. Id. The authors believed the missense variant was likely pathogenic and called for additional investigation. Id.

T.C. was admitted to the Northwell Health ED for vomiting on January 22, 2018. Pet. Ex. 24 at 5. At that time, T.C. was noted to be ventilator dependent and G-tube feed dependent. Id. Due to severe GERD and episodes of vomiting, T.C.'s G-tube was replaced with a G-J tube on January 24, 2018. Id. at 7.

On April 23, 2018, T.C. was readmitted to Northwell Health Hospital for vomiting. Pet. Ex. 37 at 1. Medical history taken by Nurse Practitioner Cristina Farrell, stated T.C. had a "GABA receptor abnormality resulting in seizure disorder." Id. at 3. T.C. had a lactose and gluten intolerance. Id. at 5. T.C. was discharged the next day after ingesting and tolerating Pedialyte. Id. at 7, 19.

Records reflecting T.C.'s visits to pediatrician Dr. Sophia Jan beginning April 27, 2018 through April 17, 2021, show that on January 28, 2021, T.C. was ventilator dependent 24 hours a day. Resp. Ex. GG at 19. Her list of active problems from 2018 to 2021 included infantile spasms, intellectual disability with epilepsy, and "Refractory Lennox-Gastaut syndrome."[13] Id. at 19-20, 100, 124, 135, 144.

On March 5, 2021, T.C. saw Dr. Sykho for a follow up of her global developmental delay, intractable epilepsy, and abnormal genetic test. Resp. Ex. FF at 12. She was seven years old. Id. Dr. Sykho had been caring for T.C. since she began having "infantile spasms" at 4 months of age. Id. Recently, T.C.'s seizures had increased due to illness. Id. T.C. was off the ventilator for part of the day, but otherwise remained ventilator dependent. Id. She had 24 hour nursing care excluding Sundays. Id. T.C. was also attending school when she had nurses available to go with her. Id. Records reveal that numerous medications have been prescribed for seizures as well as T.C.'s other medical problems. Id. at 15-16. Dr. Sykho noted that genetic testing revealed a variant of unknown significance at the GABRB2 gene. Id. at 13. Dr. Sykho's assessment was "Breakthrough seizure, Refractory Lennox-Gastaut syndrome, Global developmental delay, Dependent on ventilator, [and] Hypotonia." Id. at 16.

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[12] De novo here means a "genetic alteration that is present for the first time in one family member as a result of a variant (or mutation) in a germ cell (egg or sperm) of one of the parents, or a variant that arises in the fertilized egg itself during early embryogenesis." De Novo Mutation, Nat'l Inst. Health: Nat'l Cancer Inst. Dictionaries, https://www.cancer.gov/publications/dictionaries/genetics-dictionary/def/de-novo-mutation (last visited June 22, 2022).

[13] Lennox-Gastaut syndrome is "an atypical form of absence epilepsy characterized by diffuse slow spike waves, often with atonic, tonic, or clonic seizures and intellectual disability; there may also be other neurologic abnormalities or multiple seizure types." Lennox Syndrome, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=110889 (last visited June 8, 2022).

B. Petitioner's Affidavit and Testimony

1. Petitioner's Affidavit

In petitioner's affidavit, dated November 22, 2016, petitioner stated that "[f]rom birth, [petitioner] noticed [T.C.] had twitching and shivering type movements." Pet. Ex. 3 at ¶ 4. Petitioner stated when T.C. was one month old, petitioner noticed she "startled for no reason." Id. at ¶ 3. Petitioner mentioned her concern to T.C.'s physician and "he said it was normal for newborns to startle and it was because her nervous system was immature." Id. "One week after [T.C.]'s two month vaccines, [petitioner] started noticing her left arm twitching." Id. at ¶ 4. Petitioner brought this up with T.C.'s physician and was again told it was due to T.C.'s immature nervous system. Id.

On January 13, 2014, after her four month vaccinations, T.C. had a fever and was fussy and irritable for a couple days. Pet. Ex. 3 at ¶ 5. Petitioner was told that reaction was expected and to give T.C. Tylenol. Id. When petitioner went to feed T.C. later, petitioner "saw her eyes roll up and her body stiffen. . . . When [petitioner] picked her up she gasped for air and started crying." Id. at ¶ 6. "After that[,] [T.C.] would not stop crying for about three hours so [petitioner] decided to take her to Good Samaritan Hospital."[14] Id.

At Good Samaritan Hospital, T.C. underwent multiple tests and was diagnosed with epilepsy. Pet. Ex. 3 at ¶ 7. After discharge from the hospital, T.C. "was seizing 24/7" and would not eat. Id. at ¶ 8. Petitioner brought T.C. back to the hospital and was transferred to Cohen Children's Medical Center. Id. They repeated several tests and diagnosed T.C. with "Early Infantile Encephalopathy, Epilepsy (generalized seizures and infantile spasms)." Id.

As "of July 2016, [T.C.] has had several surgeries to have a tracheostomy placed and a [vagus nerve stimulator] implant for seizures. She is ventilator dependent . . . . She had the [vagus nerve stimulator] implant for seizures but she still has daily seizures." Pet. Ex. 3 at ¶ 10.

2. Petitioner's Hearing Testimony

During the entitlement hearing, petitioner testified regarding her own experiences and the course of T.C.'s illness. Petitioner stated T.C. was born a healthy baby and there were "no complications until about from two months to four months, [when] she started presenting some type of twitches." Transcript ("Tr.") 8. At the hearing, petitioner stated she started noticing T.C. twitching at two months of age. Tr. 20.

Petitioner stated at four months old, T.C. was administered vaccines and had "a few days of fever and discomfort." Tr. 8. Petitioner stated T.C. was inconsolable and very fussy. Tr. 11. Petitioner called her pediatrician and was told to give T.C. Tylenol every six hours. Id. Shortly

[14] T.C. was taken to Good Samaritan Hospital on January 26, 2014 for crying spells for two days and a temperature of 100.3 degrees. Pet. Ex. 5 at 7.

thereafter, T.C. had a seizure and was rushed to the hospital.[15] Tr. 8. At the hospital, T.C. "started having more of trembling seizures or twitches, like consecutive twitches." Tr. 12. The seizures were increasing in time and severity. Id.

Petitioner stated that illness triggers seizure activity for T.C. Tr. 19. However, there does not need to be a fever to trigger a seizure. Id. Seizure activity can occur from T.C. vomiting due to complications from digestion, or "even any seasonal allergy, from a little cold." Id.

At the entitlement hearing in April 2020, petitioner stated T.C. receives "twenty-four hour care, 24/7." Tr. 12. T.C. currently "is on a ventilator for breathing. She's on a G-tube for feeding. She has a [vagus nerve stimulator] device on her chest for seizures . . . . She is on several breathing treatments, and she is bedridden." Id. Petitioner stated T.C.'s last seizure was a few days before the hearing and lasted about four minutes. Tr. 14. T.C. requires petitioner to intervene and deliver rescue medication "at least once to twice a week," every week. Id. Petitioner stated T.C. has generalized seizures, myoclonic seizures, and grand mal seizures. Id.

T.C. sees her neurologist, Dr. Sykho, every two to three months. Tr. 18. T.C. has been with Dr. Sykho since she was five months old. Id. T.C. also sees her pediatrician, Dr. Jan, every four to six months. Tr. 18-19. T.C. is up to date on her standard childhood vaccinations and gets the annual flu vaccine. Tr. 25.

In regard to T.C.'s genetic testing, petitioner stated she had the same chromosome 9 deletion that the geneticists found T.C. to have. Tr. 27. Petitioner explained that the doctors "dismissed [the chromosome 9 deletion] as the cause of her illness and her medical issues." Tr. 28.

C. Expert Reports

1. Petitioner – Alan S. Levin. M.D., J.D.[16]

a. Background and Qualifications

Dr. Levin graduated medical school at the University of Illinois in Chicago in 1963, then completed a one-year fellowship in pediatric immunology at Harvard University, followed by an internship at Boston Children's Hospital. Pet. Ex. 72 at 1. He subsequently completed a postdoctoral fellowship in pediatric immunology. Id. Dr. Levin is board certified in allergy and immunology, clinical pathology, and emergency medicine. Id. Currently, Dr. Levin is part of the faculty at University of California San Francisco and conducts research on Alzheimer's disease and use of anti-cytokine treatment for Alzheimer's disease. Tr. 31. He works as a consultant and gives lectures regarding vaccines. Id. Dr. Levin received his J.D. from Golden Gate University in 1995. Pet. Ex. 51 at 1. He is a member of the California bar, Nevada bar, and

[15] Again, the date of this hospitalization was January 26, 2014.

[16] Dr. Levin filed three expert reports. Pet. Exs. 15, 16, 66.

Texas bar. Id. Dr. Levin has authored or co-authored over 60 articles and letters. Pet. Ex. 72 at 4-9. Dr. Levin has not treated a pediatric patient with seizures in approximately thirty years. Tr. 66.

b. Opinion

Dr. Levin opined "[t]his is a complicated case in which the initial neurologic abnormality was an enhanced startle reflex at one month of age." Pet. Ex. 15 at 3. "Exaggerated startle reflexes in infants can be a prodrome of seizure disorders of which the pathogenesis is probably related to an increased excitability of various parts of the infant brain." Id. The exaggerated startle reflexes were followed by twitching of the left arm, which spread over the right arm with lip smacking. Id. T.C.'s physicians initially considered T.C.'s twitching to be "neurologic immaturity." Id. at 3-4. Importantly, Dr. Levin opined that T.C.'s startle reflex began after the vaccinations and that "[n]one of the symptoms predated her vaccination. She was vaccinated on day one or two."[17] Tr. 50, 54.

Dr. Levin stated T.C. received 28 separate vaccinations prior to her January 30, 2014 seizure. Pet. Ex. 15 at 3-4. He opined that the adjuvants in the vaccines "are designed to evoke a vigorous production of proinflammatory cytokines such as IL-6 (interleukin 6) and IL-1β (interleukin 1 beta). These cytokines compromise the integrity of the endothelial cells of the blood brain barrier." Id. at 4 (citing Pet. Ex. 43).[18] According to Dr. Levin, cytokines readily cross the blood brain barrier and provoke the further production of intra-cranially produced proinflammatory cytokines by astrocytes and microglia. Id. (citing Pet. Exs. 42,[19] 46,[20] 47,[21] 48).[22] Dr. Levin opined, "[i]t is now widely accepted that these cytokines markedly reduce the excitatory threshold of various neurons." Id. (citing Pet. Ex. 44).[23] Dr. Levin opined "the purpose of vaccines is to create an inflammatory response. The problem is that under certain

[17] This is incorrect. T.C. received her first vaccination, a hepatitis B vaccination, on September 13, 2013, at four days of age. Pet. Ex. 2 at 51.

[18] Helga E. de Vries et al., The Influence of Cytokines on the Integrity of the Blood-Brain Barrier In Vitro, 64 J. Neuroimmunology 37 (1996).

[19] ManKin Choy et al., Inflammatory Processes, Febrile Seizures, and Subsequent Epileptogenesis, 14 Epilepsy Currents 15 (2014).

[20] Gang Li et al., Cytokines and Epilepsy, 20 Seizure 249 (2011).

[21] Andrey M. Mazarati, Cytokines: A Link Between Fever and Seizures, 5 Epilepsy Currents 169 (2005).

[22] Annamaria Vezzani & Tallie Z. Baram, New Roles for Interleukin-1 Beta in the Mechanisms of Epilepsy, 7 Epilepsy Currents 45 (2007).

[23] Celine Dubé et al., Interleukin-1β Contributes to the Generation of Experimental Febrile Seizures, 57 Annals Neurology 152 (2005).

circumstances, in individuals who have a genetic propensity to develop illness as a result of uncontrolled inflammatory response, then vaccines can cause adverse events." Tr. 42.

While extremely rare, Dr. Levin testified that there is an "unquestionable increase in the incidents of autoimmune disease in our children." Tr. 42. Dr. Levin cited a 2000 article by Dr. Fritz Bach[24] for support. Id. (citing Pet. Ex. 80). Bach stated, "[e]pidemiologic data provide strong evidence of a steady rise in the incidence of allergic and autoimmune diseases in developed countries over the past three decades." Pet. Ex. 80 at 1. Bach cites examples of asthma, rhinitis, atopic dermatitis, multiple sclerosis, type 1 diabetes, and Crohn's disease. Id. Bach provides little to no discussion about vaccination, but does state vaccination with bacille Calmette-Guérin did not reduce the incidence of "selected allergic and autoimmune diseases" in patients with type 1 diabetes. Id. at 7. However, Dr. Levin did not explain how the increase in incidence of autoimmune disease was relevant to his theory here. Further, Bach stated, "[i]t is important to stress that there are no solid data indicating either a positive or a negative role of vaccinations in the development of autoimmune or allergic diseases." Id.

Regarding Althen Prong One, Dr. Levin referenced the de Vries et al. article and stated, "vaccines in general cause a vigorous release of systemic proinflammatory cytokines which compromise the integrity of the endothelial cells and the integrity of the blood brain barrier. These proinflammatory cytokines provoke the production of pro-inflammatory cytokines intracranially by astroglia and microglia." Pet. Ex. 15 at 4 (citing Pet. Ex. 43). "Pro-inflammatory cytokines reduce the excitatory threshold of neurons and are a cause of aberrant firing and seizures." Id. Dr. Levin concluded that "vaccine[s] cause seizures through the action of pro-inflammatory cytokines on neurons." Id. While de Vries et al. address the effects that cytokines have on the blood brain barrier, they did not discuss vaccines, seizures, or epilepsy.

Dr. Levin testified that "[c]ytokines cause neurologic aberrations, aberrant release of neurologic signals, and in some people [] cognitive malfunction. In other people[,] [cytokines cause] [] motor malfunction. And cognitive and motor malfunctions have been labeled as seizures because that just is a description." Tr. 43-44. Dr. Levin stated that seizures are also listed on the package inserts of the vaccines.[25] Tr. 48.

When asked whether he filed medical literature to support that the theory that post-vaccination inflammation triggers central nervous system ("CNS") disorders, Dr. Levin stated, "[n]o, because it's generally recognized. It wasn't necessary to present that information." Tr.

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[24] Jean-Francois Bach, The Effect of Infections on Susceptibility to Autoimmune and Allergic Diseases, 347 New Eng. J. Med. 911 (2002).

[25] The Pediarix (DTaP, hepatitis B, IPV) package insert warns about seizures "with or without fever occurring within 3 days" of vaccination. Pet. Ex. 74 at 4. For children at risk for seizures, the package insert indicates "an appropriate antipyretic may be administered at the time of vaccination." Id. at 5. The DTaP (warning of seizures withing 3 days), hepatitis B, pneumococcal, and rotavirus (warning of seizures within 42 days) package inserts also warned about seizures. Pet. Exs. 75, 76, 78, 79. Seizures are not listed in the Hib or IPV vaccine inserts. Pet. Exs. 73, 77.

84. Respondent asked if Dr. Levin could "point to any research that supports [his] opinion," Dr. Levin replied, "[n]o, because it's in the package insert. It's general knowledge." Id.

Differentiating the etiology of fever and seizures, in response to Dr. Wiznitzer's report, Dr. Levin stated, "cytokines evoked from vaccines can cause both fever and seizures but the pathophysiology of these two disorders are completely different." Pet. Ex. 66 at 1 (citing Pet. Ex. 44). Dubé et al.[26] states fever is a systemic response to inflammation and can evoke febrile seizures. Pet. Ex. 44 at 1. Interleukin-1β ("IL-1β"), acts as a pyrogen, causing fever and can lead to enhanced neuronal excitability and decreased seizure threshold. Id. The study suggests IL-1β "contributes to the generation of human [febrile seizures], and it potentially contributes to long-lasting hyperexcitability and excitotoxicity associated with hippocampal epilepsy." Id. at 4. However, Dr. Levin testified that "cytokines can cause seizures without fever," and that "the mechanism of increased temperature and the mechanism of neuro-reactivity are biochemically different." Tr. 51. Dr. Levin opined, "[s]uccessful vaccination requires the release of cytokines from immune reactive cells. Seizures are an adverse event, unrelated to fever, that interrupt normal neuronal function." Pet. Ex. 16 at 1 (citing Pet. Ex. 68).[27]

Dr. Levin opined, "[t]herefore, vaccines cause seizures through the action of pro-inflammatory cytokines on neurons." Pet. Ex. 15 at 4. He stated that T.C.'s vaccines "directly stimulate[d] all arms of the immune system with multiple separate antigens and adjuvants at the same time. This disrupts the homeostatic balance of the immune system and causes most of the vaccine adverse events we are experiencing." Id.

In support of his opinions, Dr. Levin cited a number of medical articles. In a paper by Choy et al., the authors reviewed and described studies that investigated the role of inflammation in fever, how inflammation leads to febrile seizures, and how it may contribute to the development of epilepsy. Pet. Ex. 42. They did not discuss vaccinations.

Regarding Althen Prong Two, Dr. Levin opined that the "various vaccinations that [T.C.] received triggered her neurological abnormalities." Tr. 36. T.C. was "considered, by her treating physicians, as neurologically normal until after she received the last of her 28 separate vaccinations and adjuvants. These vaccinations were, more probably than not, a cause or a major contributor to her neurologic disease." Pet. Ex. 15 at 4. T.C.'s mother had a normal pregnancy and there was no record of seizures in utero. Tr. 49. Dr. Levin opined T.C.'s "treating physician and her obstetrician all felt that she was normal until she was vaccinated." Tr. 54. He further

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[26] Dubé et al. does not discuss vaccines. The article also does not discuss seizures independent of fever.

[27] Dr. Levin cited Graves v. Secretary of Health & Human Services, 109 Fed. Cl. 579 (2013) in support of his opinion. Pet. Ex. 68. That Opinion and Order, however, deals with the interpretation of the Vaccine Act as it relates to the statutory cap on pain and suffering damages, and does not support the proposition for which it was cited. In Graves, the infant had seizures two days after her Prevnar vaccination. No. 02-1211V, 2008 WL 4763730, at *1 (Fed. Cl. Spec. Mstr. Oct. 14, 2008). She was taken to the hospital, where she suffered status epilepticus and subsequently died. Id. at *2.

opined that none of T.C.'s symptoms "predated her vaccination. She was vaccinated on day one or two." Id.

In response to Dr. Wiznitzer's comments that T.C. had abnormal movements consistent with seizures at birth, Dr. Levin stated "[t]he record is clear [T.C.] was considered neurologically normal at birth. It was when [T.C.] was one month old, some 26 days after her first vaccination with hepatitis B, that she was noted to have an exaggerated startle reflex." Pet. Ex. 16 at 1. Dr. Levin testified, "under normal circumstances, startle reflexes are not unusual, but they could be the precursor to a seizure disorder . . . . So, it's not something that one would identify as clear evidence of the presence of a serious central nervous system disorder." Tr. 50.

Dr. Levin later stated T.C.'s inflammatory response began on day four of her life when she was administered the hepatitis B vaccine. Tr. 80. She then received a second hepatitis B vaccine on October 25, "which was prior to the development of neurologic symptomatology." Tr. 80-81. Dr. Levin testified that after T.C.'s January 13 and January 20 vaccinations, her cytokines would have been elevated for "about a week or less." Tr. 90. He opined all of T.C.'s vaccinations "evoked cytokines that are biochemically the same, so they probably all contributed" to T.C.'s epilepsy. Tr. 81.

Dr. Levin stated T.C. had elevated, proinflammatory cytokines at the time of her seizures based on the fact that she had seizures. Tr. 89. Dr. Levin stated it is "[j]ust common sense and knowledge of immunology." Tr. 90. He stated that other indications of elevated cytokines in T.C.'s medical record included a fever. Id. When asked how much inflammatory response is necessary to trigger a nervous system disorder like the one T.C. has, Dr. Levin responded that "nobody knows." Tr. 81.

Dr. Levin testified that the systemic inflammation resulting from T.C.'s vaccinations caused her to suffer a neurological event that would be viewable on an MRI. Tr. 92. However, he did not believe that T.C. had an MRI.[28] Id. Dr. Levin believed T.C. was showing signs of a CNS disorder in December 2013, as identified by T.C.'s pediatrician noting unspecified exotropia. Tr. 93.

Respondent's expert stated T.C.'s epileptic encephalopathy "was clearly present from early infancy and, by report, did not worsen in the immediate days after any of her immunizations. Rather, it became more evident in conjunction with an upper respiratory infection." Resp. Ex. H at 2. Dr. Levin proposed this statement by Dr. Wiznitzer "indicates that he agrees with me that the patient was born with the genetic defect that would have remained silent but for the identical cytokines produced by the vaccines (in my opinion) and/or by the respiratory infection (Dr. Wiznitzer's opinion)." Pet. Ex. 66 at 2. Dr. Levin testified that the upper respiratory infection and possible other exposure to pathogens could have served as another inflammatory process to trigger T.C.'s disorder. Tr. 96. While Dr. Levin opined both T.C.'s upper respiratory infection and vaccines triggered her neurological abnormality, he

[28] This is incorrect. T.C. did have an MRI, on February 3, 2014, without contrast, and it showed "[n]o evidence of acute intracranial pathology." Pet. Ex. 5 at 92-93. Additionally, on February 10, 2014, a repeat MRI without contrast revealed unremarkable findings. Id. at 255.

believed that the vaccines initiated the systemic inflammation, which was compounded by infection. Tr. 107.

Dr. Levin agreed with the diagnosis of epileptic encephalopathy resulting from a GABRB2 variant. Tr. 94. He opined that the vaccines T.C. received "triggered a genetic predisposition to her seizure disorder, and but for . . . those vaccinations, the seizure disorder would not have presented at the time that it did." Tr. 57. He also opined the "idea that a genetic mutation causes a disease process is unscientific. If this particular genetic mutation in this child caused her or triggered her disease process, she would have been seizing in utero." Tr. 37. Dr. Levin stated, "Dr. Wiznitzer believes that the disease process was latent until she developed a viral upper respiratory infection." Tr. 37. "So, Dr. Wiznitzer believes that the cytokines that are released by the viral infection triggered the disease. I believe that the cytokines that were released by the vaccination triggered the disease. I believe that we're both right."[29] Tr. 38. "Genetic mutations don't cause disease. They cause disease when they're triggered." Tr. 43. However, Dr. Levin agreed that T.C.'s treating physicians believe that her genetic mutation is associated with her neurologic disorder. Tr. 97. And he was unable to reference any medical records to show that any of T.C.'s treating physicians attributed her epileptic encephalopathy to her vaccinations. Tr. 97-98.

As for the genetic test results, Dr. Levin testified that T.C.'s genetic tests showed "a genetic abnormality on chromosome 9," which "alters the capacity . . . to appropriately process certain proteins." Tr. 69-70. He also agreed that testing revealed that T.C. had a variant to the GABRB2 gene and that the variant was de novo (as opposed to inherited). Tr. 70. Dr. Levin stated that when petitioner testified that "she has the same mutation" as her daughter, he was unclear what she "was referring too." Id.

However, Dr. Levin also testified that given that T.C.'s mother has the "same mutation[30] and is totally asymptomatic, and has given birth to two asymptomatic children . . . there's something more than just the mutation that caused [T.C.'s] illness." Tr. 41. He agreed that T.C.

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[29] Later Dr. Levin also agreed that T.C.'s "upper respiratory viral infection" could have served as a trigger for her disease process. Tr. 96. He also testified that the vaccines compounded by the upper respiratory infection "evoked the neurologic abnormality." Tr. 107. Dr. Levin did not proffer a theory as to how the vaccine and viral infection worked in tandem to trigger T.C.'s seizures.

[30] This is incorrect with regard to T.C.'s GABRB2 genetic variant. T.C. has two genetic abnormalities. The first was discovered during T.C.'s medical genetics assessment at Children's Medical Center of New York on June 5, 2014, which showed an interstitial deletion of "uncertain significance" that was found to be maternally inherited. Pet. Ex. 11 at 6. Further testing done November 22, 2016 (molecular genetics test done at Columbia University Medical Center) showed a GABRB2 abnormality of "uncertain clinical significance," which was "a de novo finding." Pet. Ex. 52 at 2. The fact that it was a de novo finding indicates it was not inherited. Dr. Levin's testimony does not account for the fact that T.C.'s GABRB2 abnormality is de novo, not inherited, and not shared with her mother. For a more complete explanation of T.C.'s two different genetic abnormalities by Dr. Wiznitzer, see Tr. 126-38, 224-25.

was likely born with the variant. Tr. 72. Dr. Levin also agreed that vaccination was "irrelevant in terms of the development of this disorder," the GABRB2 gene variant. Id.

Regardless of the variant's origins, Dr. Levin stated the GABRB2 variant "clinically manifests itself as [CNS] disorders." Tr. 72. He believed that T.C.'s genetic variant caused a genetic propensity to develop illness, specifically her central nervous system/seizure disorder, after an inflammatory response. Tr. 75-80. He testified that T.C.'s developmental delay and cortical visual impairment were due to the seizure disorder. Tr. 80.

Dr. Levin also found "the temporal association between the vaccinations and the neurological disorder is appropriate." Pet. Ex. 15 at 4. Dr. Levin established a timeline indicating T.C. was "vaccinated with [h]epatitis B on day 4 of life. She received the second [h]epatitis B vaccination on day 46 of life. She received vaccinations with 22 separate antigens and adjuvants on day 65 of life. She received 6 more vaccinations with adjuvants in the next 67 days of her life." Id. He opined that the timing of all of these vaccinations, "is totally consistent with activation of innate immune responses causing the production of pro-inflammatory cytokines as well as adaptive immune T and B cells further producing cytokines." Id.

Dr. Levin explained that shortly after vaccination, there is "the innate immune response and the release of certain cytokines, and then if the vaccination is successful, you have the adaptive immune response that happens within a week or two after the initial vaccination and happens days or hours after subsequent vaccination with the same or similar antigens." Tr. 46. "The innate immune response is immediate, almost immediate, within hours. And then the adaptive immune response takes initially a week or two, and then it lasts for probably a month, maybe a month and a half but usually it's not very serious after the first three or four days." Tr. 82.

Dr. Levin testified T.C. had seizure activity on October 9, 2013,[31] within five days of vaccination, which manifested as an exaggerated startle reflex. Tr. 99. "[A]t the time [it] probably was not considered to be abnormal, but now in hindsight, [Dr. Levin] indicates that she was beginning to develop the seizure disorder." Id. However, October 9 was three weeks after T.C.'s first hepatitis B vaccination. Id. It was not five days after the first vaccination.

Dr. Levin concluded, "[t]o discount the contribution of 28 separate vaccinations and their adjuvants in the first 4 months of life to this child's neurological illness is scientifically disingenuous." Pet. Ex. 16 at 2. "[T]o a reasonable degree of medical certainty," Dr. Levin opined "the vaccines that [T.C.] received triggered a genetic predisposition to her seizure disorder, and but for that—those vaccinations, the seizure disorder would not have presented at the time it did." Tr. 57.

[31] Dr. Levin does not state the basis for his opinion, but appears to be relying on a portion of petitioner's affidavit, wherein petitioner averred that T.C. startled at one month. Pet. Ex. 3 at ¶ 3. However, in the same affidavit, petitioner stated that T.C. had twitches and shivering type movements from birth. See id. at ¶ 4.

2. Respondent – Dr. Max Wiznitzer[32]

a. Background and Qualifications

Dr. Wiznitzer obtained his medical degree from Northwestern University in 1977. Resp. Ex. B at 1. He then completed a residency in pediatrics at Children's Hospital Medical Center in Cincinnati; a fellowship at the Cincinnati Center for Developmental Disorders; a fellowship in pediatric neurology at the Children's Hospital of Philadelphia; and a fellowship in higher cortical functions at the Albert Einstein College of Medicine. Id. at 1-2. He is a pediatric neurologist at University Hospitals of Cleveland, as well as an associate professor of several subjects at Case Western University. Id. at 2. He is board-certified in pediatrics; psychiatry and neurology (with a special qualification in child neurology); neurodevelopmental disabilities; and medical examination. Id. at 5. He is a journal reviewer and on the editorial board of several journals, including Lancet Neurology and Pediatric Neurology. Id. at 6. He has authored or co-authored over 80 journal articles and book chapters. Id. at 14-21. Dr. Wiznitzer has an active clinical practice interpreting EEGs and treating pediatric patients who have seizure disorders and epileptic encephalopathies. Tr. 118.

b. Opinion

i. Althen Prong One

Regarding petitioner's theory of causation, Dr. Wiznitzer disagreed with a number of Dr. Levin's opinions. First, he disagreed that cytokines produced from vaccination can compromise the integrity of the endothelial cells of the blood brain barrier. Tr. 178. While Dr. Wiznitzer did agree that very high levels of cytokines can compromise the blood brain barrier, he disagreed that vaccinations would cause a sufficient number of cytokines to do so. Tr. 178-81.

Additionally, Dr. Wiznitzer also took issue with Dr. Levin's statement that after vaccination, cytokines have a cumulative effect. Tr. 195. As explained by Dr. Wiznitzer, cytokines "don't sit around forever." Id. The only way that cytokines would continue to be present is if there is something that "continues to set them off," but "that is not what [Dr. Levin has] proffered in his testimony." Id.

Dr. Wiznitzer next discussed that Dr. Levin's theory associating vaccination with epilepsy is not supported by the medical literature filed by petitioner. Resp. Ex. A at 10. Dr. Wiznitzer opined many of petitioner's articles are irrelevant to T.C. because she did not have febrile seizures close in time to any of her vaccinations. Id. at 10-11 (citing Pet. Exs. 42, 44, 48). For example, Choy et al. discuss inflammation markers, such as IL-1β, that are known triggers of fever and have also been implicated as contributors to the onset of febrile seizures. Pet. Ex. 42 at 1. Dubé et al. similarly state that fever can provoke febrile seizures and IL-1β cytokines are implicated in contributing to fever-induced hyperexcitability underlying febrile seizures. Pet. Ex. 44 at 1. Vezzani and Baram's research also supports the role of IL-1β in inducing fever that can promote the occurrence of febrile seizures. Pet. Ex. 48 at 3.

[32] Dr. Wiznitzer filed three expert reports. Resp. Exs. A, H, BB.

Moreover, Dr. Wiznitzer opined that T.C. did not have any seizure attributable to vaccination that significantly aggravated her epileptic encephalopathy. Tr. 187. When responding to the hypothetical question, would T.C.'s outcome be different if she never had a fever in her first year of life, Dr. Wiznitzer replied, "[i]t would not." Tr. 186. Based on his medical training, Dr. Wiznitzer opined that due T.C.'s type of epilepsy and brain pathology, her outcome would not be affected by the fevers or seizures she had in her first year of life. Tr. 186-88. Dr. Wiznitzer stated that other children with similar mutations in the same location have analogous pathologies—it "is just the evolution of this epilepsy." Tr. 187.

Additionally, petitioner's medical literature, the Facini et al., Sanz and Di Virgilio,[33] and Lopez-Castejon and Brough[34] articles, did not discuss epilepsy or vaccination. Resp. Ex. A at 10 (citing Pet. Exs. 45, 49, 50). Facini et al. provided an overview of the clinical features of neonatal paroxysmal motor phenomena, or "sudden, mostly short-lasting involuntary movements and alterations of muscle tone, involving various parts of the body." Pet. Ex. 45 at 1. The authors stated the movement could be due to an immature CNS or could be pathological or epileptic in origin. Id. Sanz and Di Virgilio and Lopez-Castejon and Brough discuss the immunological mechanisms of IL-1β as a potent proinflammatory cytokine. Pet. Ex. 49 at 1; Pet. Ex. 50 at 1. Again, they did not mention vaccination or epilepsy.

ii. Althen Prong Two

Dr. Wiznitzer initially laid out a number of points regarding T.C.'s diagnosis and clinical history. Resp. Ex. A at 10. First, he noted that T.C.'s twitches were present since birth, and were later identified as seizures after an EEG study. Id. Second, T.C.'s seizure semiology included "infantile spasms, myoclonic seizures, and tonic seizures." Id. Third, her seizures increased during febrile illnesses, but also occurred independent of fever or illness. Id.

Notably, Dr. Wiznitzer opined that T.C. did not have a documented fever after receipt of her vaccinations on January 13 or 20, 2014. Resp. Ex. A at 10. However, T.C. had an upper respiratory infection with fever at the time of her emergency room visit on January 26, 2014. Id. Dr. Wiznitzer opined that "[a] diagnosis of an epileptic encephalopathy . . . was clearly present from the time of birth, and by report, did not worsen in the immediate days after any of her immunizations. Rather, it became more evident in conjunction with an upper respiratory infection at the end of January 2014." Id.

Factually, Dr. Wiznitzer disagreed with some of Dr. Levin's statements and opinions that were not supported by the contemporaneous medical records. Resp. Ex. A at 11-12. Dr. Wiznitzer disagreed that T.C.'s twitches, noted from birth, were evidence of an excessive startle reflex, but instead, he opined that they were due to her epilepsy. Id. at 12. Additionally, he

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[33] Juana M. Sanz & Francesco Di Virgilio, Kinetics and Mechanism of ATP-Dependent IL-1 β Release from Microglial Cells, 164 J. Immunology 4893 (2000).

[34] Gloria Lopez-Castejon & David Brough, Understanding the Mechanism of IL-1 β Secretion, 22 Cytokine Growth Factor Rev. 189 (2011).

opined that the allegation that T.C. had new left arm twitching after the November 13, 2013 vaccinations was not reported in her contemporaneous medical records.[35] Id. Additionally, according to Dr. Wiznitzer, Dr. Levin's statement that T.C. had fever for two days after the January 13, 2014 vaccinations is not supported by the contemporaneous medical records.[36] Id.

Instead of developing epilepsy after vaccination, Dr. Wiznitzer opined that T.C. was born with her condition of epileptic encephalopathy. Tr. 169. He testified that in many cases, children with genetic epilepsies are normal during pregnancy. Tr. 170. "In fact, clinically, the children can look reasonably okay in the first months of life, depending on what the timing is, and then basically the epilepsy starts, and all the delays associated with it basically evolve." Id. Dr. Wiznitzer emphasized that he has "seen that pattern over and over and over again." Id.

Dr. Wiznitzer opined that the cause of T.C.'s epileptic encephalopathy is "a pathogenic mutation of the GABRB2 gene."[37] Tr. 126. He cited a number of articles to support his opinion and explain that T.C.'s epileptic encephalopathy is genetic in nature and not caused by her vaccinations. Resp. Ex. A at 12. Berg et al. describes epileptic encephalopathy and "that the epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology alone (e.g., cortical malformation), and that these can worsen over time." Resp. Ex. C at 7. "Epileptic encephalopathy can present along a continuum of severity and may occur at any age. The phenomenon is most common and severe in infancy and early childhood, where global and profound cognitive impairment may occur." Id. at 8. The authors state, "[t]he concept of genetic epilepsy is that the epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder." Id. at 5. "Designation of the fundamental nature of the disorder as genetic does not exclude the possibility that environmental factors (outside the individual) may contribute to the expression of disease." Id.

Scheffer et al.[38] stated, "[m]any epilepsy syndromes associated with encephalopathy have a genetic etiology . . . where there is marked genetic heterogeneity, and [e]pileptic encephalopathy with continuous spike-and-wave during sleep (CSWS), where the first genes have begun to emerge." Resp. Ex. G at 7. "Equally, such syndromes may have an acquired cause such as hypoxic-ischemic encephalopathy or stroke, or may be associated with a malformation of cortical development that may also have a genetic or acquired etiology." Id.

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[35] The first reference to T.C.'s left arm twitching was on January 31, 2014. Pet. Ex. 5 at 67.

[36] The contemporaneous medical records from January 13 to January 20, 2014 do not document that T.C. had any fever during this timeframe. See Pet. Ex. 2 at 35-37.

[37] Dr. Wiznitzer explained that both T.C. and her mother had a "deletion on Chromosome 9" that was found on testing, but that is different than the GABRB2 genetic mutation which T.C. has, which is de novo, and located on Chromosome 5, and is the focus of Dr. Wiznitzer's testimony regarding the cause of T.C.'s epileptic encephalopathy. Tr. 224-25.

[38] Ingrid E. Scheffer et al., ILAE Classification of the Epilepsies: Position Paper of the ILAE Commission for Classification and Terminology, 58 Epilepsia 512 (2017).

"The concept of an epileptic encephalopathy can also be applied to single gene disorders." Id. "Many of these severe genetic disorders also have developmental consequences arising directly from the effect of genetic mutation, in addition to the effect of the frequent epileptic activity on development." Id. at 8.

McTague et al. report "[e]pileptic encephalopathies of infancy and childhood comprise a large, heterogeneous group of severe epilepsies characterized by several seizure types, frequent epileptiform activity on EEG, and developmental slowing or regression." Resp. Ex. E at 1. "The onset of epileptic encephalopathies might occur against a background of normal or delayed development." Id. The authors stated, "[a] minority of cases undoubtedly have symptomatic causes in which a child has a structural aetiology such as a stroke or hypoxic-ischaemic encephalopathy underlying their epileptic encephalopathy." Id. at 4. However, "[a] genetic cause has been identified in many different epileptic encephalopathies with many previously unknown genes emerging. The genetic causes of epileptic encephalopathies are heterogenous; de-novo mutation in the affected individual are most commonly reported." Id.

Dr. Wiznitzer explained that T.C. "had no identifiable brain abnormalities on MRI, which would be expected with an acquired cause, and had seizures and involuntary movements, which occur in some of the genetic disorders associated with epileptic encephalopathy." Resp. Ex. A at 12. "She has a history of body twitches from the time of birth, which are probably [myoclonic] seizures and which can occur with epileptic encephalopathy." Id. "The clinical identification of her epilepsy at age 4 months is consistent with the evolution of an epileptic encephalopathy, including the appearance of infantile spasms, and, therefore, [vaccination was] not the causation or exacerbation [as] claimed by Dr. Levin." Id. at 12-13.

Additionally, the Columbia University Diagnostic Sequencing Study of Genetic Disorders test results on T.C. revealed a de novo heterozygous variant on the GABRB2 gene. Resp. Ex. H at 2. Dr. Wiznitzer explained, "the $GABA_A$ receptors are the major inhibitory neurotransmitter receptors" of the brain. Id. at 3. Loss of function of these receptors can lead to imbalance in excitation-inhibition with an excess of excitation, which can lead to seizures, movement disorders, and developmental delay/intellectual disability." Id. (citing Resp. Exs. I,[39] J).[40] In utero, these GABA receptors are excitatory, but at birth GABA receptors are inhibitory. Tr. 128. Dr. Wiznitzer testified that more GABA receptors grow as an individual ages. Id.

More specifically, Dr. Wiznitzer testified that "the GABRB2 gene codes for one of the subunits of the $GABA_A$ receptor." Tr. 126. The $GABA_A$ receptor "is the major inhibitory nerve transmitter receptor in the body." Id. GABA, a neurotransmitter, binds at a "specific location . . . between an alpha and beta subunit." Tr. 127. The $GABA_A$ receptor is made of "five subunit proteins" that combine to "form a cylinder . . . through which chloride ions move." Id.; see also Resp. Ex. DD. "[T]he movement of the chloride ions [] causes the inhibitory effect on the

[39] H. Möhler, GABAA Receptor Diversity and Pharmacology, 326 Cell Tissue Research 505 (2006).

[40] Erwin Sigel & Michael E. Steinmann, Structure, Function, and Modulation of GABAA Receptors, 287 J. Biological Chemistry 40224 (2012).

transmission of electrical signal along the nerve." Tr. 127. After birth, the system evolves over time, so that at two to four months of age, there are more $GABA_A$ receptors than are present at birth. Tr. 128. If the $GABA_A$ receptor does not properly inhibit, there is "an imbalance between excitation and inhibition . . . in the nervous system." Tr. 129. The β2 subunit, which is "the dysfunctional gene in T.C." is a "de novo change[] in the genetic code that [is] deleterious . . . [and] lead[s] to an imbalance in excitation and inhibition." Tr. 131. There is more excitation because there is less inhibition, and this causes epilepsy. Tr. 131-32.

Dr. Wiznitzer testified that there is "a list of genes that have been identified so far as being associated with epilepsy. And . . . GABRB2 is one of them." Tr. 132. Others included de novo mutations "in GABRA1, GABRA2, GABRA5, GABRB1, GABRB2, GABRIB3[,] and GABRG2 . . . found in cases of epileptic encephalopathies with a broad phenotypic range that includes early onset (infantile) epileptic encephalopathy." Resp. Ex. H at 3. Dr. Wiznitzer cited numerous articles and medical literature to demonstrate that de novo GABRB2 variants are associated with epilepsy. Id. at 3-5.

Srivastava et al. (the article that was attached to T.C.'s genetic results), published in 2014, reported on a twelve-year-old who had onset of febrile seizures at age nine months that continued to recur and evolve into nonfebrile seizures. Resp. Ex. H at 3 (citing Resp. Ex. L). The febrile seizures in infancy resolved, but the child went on to develop generalized epilepsy. Resp. Ex. L at 6. This was the "first report of a missense mutation in the β2 subunit of the $GABA_A$ receptor as a cause of genetic epilepsy and intellectual disability." Id. at 7.

Ishii et al.[41] reported that a de novo heterozygous missense mutation in the GABRB2-encoded β2 subunit of the $GABA_A$ was associated with severe epileptic encephalopathy. Resp. Ex. P at 7. Yang et al.[42] identified GABRB2 variants in fifteen patients in their article, published in 2020. Resp. Ex. H at 5 (citing Resp. Ex. W). They found that the most common phenotype associated with GABRB2 variants included patients with early onset of seizures and fever sensitivity. Resp. Ex. W at 1. Seizure onset usually occurred in the first few years of life, with most having "epilepsy, intellectual disability, . . . [and] developmental and epileptic encephalopathy." Tr. 137. EEG reports may show hypsarrhythmia, "a very severe epilepsy pattern." Tr. 138. The "location where the mutation or where the gene variant occurs appears to affect the severity of the clinical picture in their patients." Tr. 139. All severe phenotypes[43] in

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[41] Atsushi Ishii et al., A De Novo Missense Mutation of GABRB2 Causes Early Myoclonic Encephalopathy, 54 J. Med. Genetics 202 (2017).

[42] Ying Yang et al., Phenotypic Spectrum of Patients with GABRB2 Variants: From Mild Febrile Seizures to Severe Epileptic Encephalopathy, 62 Developmental Med. Child Neurology 1 (2020).

[43] Dr. Wiznitzer defined phenotype as "the clinical picture of the individual." Tr. 141. Phenotype is defined by Dorland's as "the observable morphologic, biochemical, and physiologic characteristics of an individual, either in whole or with respect to a single or a few traits." Phenotype, Dorland's Online Med. Dictionary, https://www.dorlandsonline.com/dorland/definition?id=38503 (last visited June 9, 2022).

the study had the mutation between site 245 and 303, "which is the number of the amino acid on the protein, . . . in the transmembrane region." Id. Hamdan et al. also report that "variants [] clustered in the positions 244 to 304,[44] which encompassed three transmembrane domains . . . [were] associated with severe global developmental delay or intellectual disability." Tr. 139-40.

Hamdan et al. studied a group of individuals with unexplained developmental and epileptic encephalopathy and pharmaco-resistant seizures and were able to provide a causal link between the developmental and epileptic encephalopathy and GABRB2 gene mutations. Resp. Ex. H at 4 (citing Resp. Ex. R). The authors "identified [eleven] individuals with GABRB2 de novo mutations, all of which were predicted to be damaging. All individuals had moderate to severe intellectual disability. Within the first year of life, most children developed refractory seizures that sometimes evolved into myoclonic status epilepticus or nonconvulsive status epilepticus." Id. "Some developed focal seizures, tonic seizures, atonic seizures, and/or rarely generalized tonic-clonic seizures. For [five] of the individuals, the epilepsy remained refractory despite multiple drug trials." Id. Hamdan et al. state, "[c]ollectively, the previously and presently reported individuals with [de novo mutations] in GABRB2 confirm that the de novo missense mutations in GABRB2 can cause a [developmental and epileptic encephalopathy] phenotype." Resp. Ex. R at 9 (emphasis omitted). Hamdan et al., like Yang et al., also stated variants that were clustered in the positions 244 to 304 were associated with severe outcomes, such as global developmental delay or intellectual disability. Tr. 139-40.

El Achkar et al. characterized "the phenotypic spectrum and functional consequences associated with variants in the gene GABRB2, coding for the γ-aminobutyric acid type A ($GABA_A$) receptor subunit β2." Resp. Ex. CC at 1. The authors opined "GABRB2-related epilepsy ranges broadly in severity from genetic generalized epilepsy to developmental and epileptic encephalopathies. Developmental disability and movement disorder are key features." Id. The authors found that "[m]issense variants were located in regions of the protein that are intolerant to functional variation." Id. at 6. Dr. Wiznitzer testified this region is the same region identified by Yang et al. and Hamdan et al. Tr. 140. He opined that T.C.'s mutation is in the same location. Tr. 140, 151. T.C.'s mutation results in "changing the C to a T in the DNA code," so that "instead of having a proline amino acid at site 252, . . . [there is] a leucine amino acid." Tr. 151. Based on current knowledge and predictive algorithms, Dr. Wiznitzer opined that T.C.'s mutation is "predicted to be deleterious." Tr. 153. Further, based on the testing done by El Achkar et al., this mutation causes "a loss of function" and results in "an imbalance between excitation and inhibition," which will cause seizures and developmental impairment. Tr. 156-57. Additionally, the majority of those with the mutation have "cortical visual impairment" and profound development problems. Tr. 159.

Dr. Wiznitzer concluded that T.C.'s developmental and epileptic encephalopathy is due to her de novo pathogenic GABRB2 gene mutation. Resp. Ex. H at 6-7; Tr. 168. Dr. Wiznitzer testified, T.C.'s mutation and clinical presentation is similar to individuals studied in the medical

[44] T.C.'s mutation is a P252L missense variant at position 252 in the GABRB2 protein. Pet. Ex. 52 at 2.

literature as demonstrated by the Columbia study results.[45] Tr. 160-61, 164-67. Therefore, he does not believe that her epileptic encephalopathy was caused or aggravated by any of her immunizations. Tr. 163.

The fact that T.C.'s mom had a normal pregnancy, and that T.C. had a normal birth, and that clinically, T.C. did well in the first few months of life is, according to Dr. Wiznitzer, not unexpected. Tr. 170. He explained that before birth, the GABA receptors are immature, and so the clinical changes are not seen until the GABA receptors mature. Id. According to the records, T.C. had twitching on and off after birth.[46] Id. Dr. Wiznitzer opined that T.C. was born with the deleterious gene mutation, and had twitching since birth, abnormal eye movements, feeding problems, and increased movement, evidencing a "clinical evolution of her genetic epilepsy." Tr. 171. Further, at the later part of January 2014, she was described as having a developmental disorder. Tr. 173. Her MRI was normal, and did not show inflammation, or "evidence of a breakdown of the blood-brain barrier." Id. Instead of inflammation, Dr. Wiznitzer opined that T.C.'s problem was at a microscopic level, at the level of the nerves, due to her mutation. Id.

Additionally, Dr. Wiznitzer disagreed with Dr. Levin's opinion that the current vaccine schedule overwhelms the immune system, or that it did so in T.C. Tr. 181. There is no evidence that her immune system was "overwhelmed in any way" or that her immune system was not working properly. Id. She did not have evidence that her immune system could not fight infections, she did not have abnormal MRIs, she did not have dysfunction of her endocrine system. Tr. 182.

Further, Dr. Wiznitzer disagreed that any vaccinations were contraindicated for T.C. Tr. 185. To the contrary, it is important that she receive vaccinations to protect her against preventable infections which cause illness and fever. Id.

Dr. Wiznitzer disagreed that T.C.'s clinical course was consistent with Dr. Levin's opinion of vaccine causation. Resp. Ex. A at 12-13. T.C.'s twitches were present after birth, then she began receiving her vaccinations, including her hepatitis B vaccines at four days, and the second one in October. Id. at 12. She then received her first set of vaccinations in November, followed by the second set in January. Id. Dr. Wiznitzer opined that there was "no description during that time of any significant worsening of function in the days after those vaccinations." Tr. 174. Using the theory and timeline proposed by Dr. Levin, "where cytokines should be elevated in the first week" after vaccination, Dr. Wiznitzer opined there "was no real

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[45] At the hearing, Dr. Wiznitzer testified that (as of the date of the hearing) there have been 73 deleterious variants affecting the β2 subunit of the $GABA_A$ receptor reported. Tr. 150.

[46] Dr. Wiznitzer testified that according to T.C.'s mother, T.C. had twitches since birth, which he interpreted to mean "right at the time." Tr. 250. Since T.C. received her first hepatitis B vaccination at four days of age, he believed that T.C.'s twitches began before she received her first vaccination. Id. He noted that the physician who evaluated T.C. documented the past medical history was significant for "benign myoclonic jerks of mostly left shoulder that occurred off and on since birth." Tr. 264 (citing Pet. Ex. 5 at 69). The term "twitching" was also referenced in the same record. Pet. Ex. 5 at 67.

clinical change in terms of seizures or development that was reported during that time." Id.

The change or deterioration seen clinically in T.C. occurred on January 30, 2014, "with the appearance of an obvious tonic seizure . . . that occurred in conjunction with her upper respiratory infection." Tr. 174. Dr. Wiznitzer opined that illness can provoke seizure activity, so this course was not surprising. Id. The seizure did not occur within the first week, but occurred ten days after her IPV vaccination, and 17 days after DTaP, Hib, and rotavirus vaccines administered on January 13, 2014. Tr. 175. Moreover, the type of seizure T.C. had was consistent with those reported in others who have GABRB2 associated epileptic encephalopathy. Id.

Dr. Wiznitzer disagreed with Dr. Levin that a trigger is necessary for clinical symptoms to present in children with a GABRB2 genetic variant. Tr. 177. Fever may provoke a seizure, but the "underlying pathology in the brain is . . . an unfixable imbalance between excitation and inhibition." Tr. 177. Illness may also lower the seizure threshold so that seizures occur more readily. Tr. 251. Dr. Wiznitzer explained, however, that the genetic variant at issue is not triggered, because it is present at birth. Tr. 255.

iii. Althen Prong Three

Dr. Wiznitzer opined T.C.'s epileptic encephalopathy manifested when she was noted to have exotropia at her December 14, 2013 well-baby checkup. Resp. Ex. A at 12. He stated her epileptic encephalopathy predated her vaccinations as shown by her twitching, as well as her abnormal eye movement and feeding issues. Tr. 171. When T.C. was first admitted to the hospital, "she was described as having a lot of movement, . . . suggesting that the movement disorder was there but probably was not as evolved to become clinically evident." Tr. 172-73. Additionally, there were no associated brain MRI abnormalities. Tr. 173. T.C., however, had EEG abnormalities (burst suppression pattern and frequent epileptiform discharges, depending on age of the EEG study), and she had clinical seizures (infantile spasms, myoclonic, focal, and generalized tonic-clonic seen over time). Tr. 172-73; Resp. Ex. A at 12.

Further, Dr. Wiznitzer opined the latency between vaccination and T.C.'s seizures make it unlikely that the vaccines were a causative factor. Tr. 268-70. For the DTaP vaccination, if a child had a febrile seizure due to fever related to vaccination, Dr. Wiznitzer testified it would occur within the first three days after vaccination. Tr. 269. This time frame would also apply to the Hib and pneumococcal vaccinations. Id. Dr. Wiznitzer would not expect fever to occur after hepatitis B vaccinations, but if it did, again, it would happen within three days at the most. Tr. 269-70. He testified that fevers do not usually occur after IPV or rotavirus vaccinations. Id.

VI. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The

Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

B. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records). Contemporaneous medical records, "in general, warrant consideration as trustworthy evidence." See Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir.

1993).

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, petitioner must prove either (1) that T.C. suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that T.C. suffered an injury that was actually caused by a vaccination. See §§ 13(a)(1)(A), 11(c)(1); Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Because petitioner does not allege that T.C. suffered a Table Injury, she must prove that the vaccines T.C. received caused her injury. To do so, she must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccines and T.C.'s injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccines were the reason for T.C.'s injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccines and T.C.'s injury ("Althen Prong Three"). § 13(a)(1); Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. The petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in petitioner's favor).

D. Causation Analysis

1. Althen Prong One

Under Althen Prong One, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

Petitioner's expert, Dr. Levin, proposes that vaccinations, specifically the adjuvants in vaccines,[47] evoke the production of proinflammatory cytokines which cross the blood brain barrier, resulting in further production of proinflammatory cytokines (astrocytes and microglia) that significantly reduce the excitatory threshold of certain neurons. He opines that in infants with a genetic propensity to develop a seizure disorder, these proinflammatory cytokines trigger seizure disorders such as epilepsy. Dr. Levin further opines that the antigens and adjuvants of 28 vaccinations, administered over the period of time relevant here, activated the innate immune responses causing the production of proinflammatory cytokines, as well as the adaptive immune T and B cells, which also produce cytokines. He explains that the innate immune response is almost immediate, and occurs within hours, while the adaptive immune response[48] takes a week, and lasts about a month, although it is not very serious after the first three to four days.

Medical literature filed by petitioner supports the proposition that proinflammatory cytokines may play a role in the development of fever, which may lead to seizures and epilepsy. For example, Vezzani and Baram discuss the following hypotheses related to cytokines: They may be released during an inciting event which may promote a hyperexcitable state; they may contribute to seizure-evoked neuronal cell death; and they may play a role in febrile seizures. See generally Pet. Ex. 38. Choy et al. explain that inflammatory mediators (cytokines) are present following febrile seizures, as well as during established epilepsy, suggesting they may contribute to the etiology of seizures. Pet. Ex. 42. Notably, however, the authors state that while prolonged or focal febrile seizures may increase the risk of temporal lobe epilepsy,[49] they conclude that the "majority of clinical studies suggest that there is little enduring adverse impact

[47] Dr. Levin did not identify any specific adjuvant at play, nor did he provide any evidence to show that adjuvants cause release of proinflammatory cytokines that remain present over time, or accumulate, so as to result in seizures and epilepsy.

[48] Dr. Levin did not explain or develop the aspect of his theory which involved the adaptive immune response.

[49] T.C. has not been diagnosed with temporal lobe epilepsy.

of short febrile seizures on the developing brain." Id. at 3. The literature does not support the notion that afebrile seizures are triggered by vaccination, or that afebrile seizures play a role in triggering epilepsy.[50] And the facts of this case do not establish that there was a vaccine proximate fever associated with any seizure prior to the diagnosis of epilepsy.

Moreover, Dr. Levin suggests that there is a cumulative effect of cytokines after vaccination, and that 28 separate vaccinations and their adjuvants, over a period of four months, caused her epilepsy. See Pet. Ex. 15 at 4; Pet. Ex. 16 at 2; Tr. at 57. This idea, however, is inconsistent with Dr. Levin's opinion that the release of proinflammatory cytokines is almost immediate, and within hours and days of vaccination. Tr. 82. Dr. Levin did not provide any evidence to show that vaccine-induced cytokines remain present in the central nervous system for more than a short period of time after vaccination. Nor did he provide any evidence that the cytokines from a vaccination accumulate or form a cumulative effect over time, so as to cause seizures or epilepsy at a future date. Instead, de Vries et al. note cytokines are released after injury or inflammation, and Choy et al. state that after release, cytokines remain elevated for 24 to 48 hours. Pet. Ex. 43 at 1; Pet. Ex. 42 at 4.

In addition to suggesting that proinflammatory cytokines have a cumulative effect, Dr. Levin also opines that vaccines cause an "uncontrolled inflammatory response" which can lead to illness in children with genetic propensity. Tr. 42. But he did not explain what he meant by an "uncontrolled inflammatory response" or how vaccines can cause such a response. Moreover, he did not provide any evidence to support this opinion. As such, Dr. Levin's opinion is vague, conclusory, and not developed through the literature that he cited.

When evaluating whether petitioners have carried their burden of proof, special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *31 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, decision aff'd, 141 Fed. Cl. 138 (2018), aff'd, 945 F.3d 1362 (Fed. Cir. 2020). The undersigned will not rely on "opinion evidence that is connected to existing data only by the ipse dixit of the expert." Prokopeas v. Sec'y of Health & Hum. Servs., No. 04-1717V, 2019 WL 2509626, at *19 (Fed. Cl. Spec. Mstr. May 24, 2019) (quoting Moberly, 592 F.3d at 1315). Instead, special masters are expected to carefully scrutinize the reliability of each expert report submitted. See id.

In addition to offering vague and conclusory opinions, Dr. Levin's opinions were also misleading or irrelevant, including his inference that vaccinations cause an increase in

[50] Dr. Levin cited Graves v. Secretary of Health & Human Services, 109 Fed. Cl. 579 (2013) in support of his opinion. Pet. Ex. 68. That Opinion and Order, however, deals with the interpretation of the Vaccine Act as it relates to the statutory cap on pain and suffering damages, and does not support the proposition for which it was cited. The underlying facts are also distinguishable. In Graves, the infant had seizures two days after her Prevnar vaccination. No. 02-1211V, 2008 WL 4763730, at *1 (Fed. Cl. Spec. Mstr. Oct. 14, 2008). She was taken to the hospital, where she suffered status epilepticus and subsequently died. Id. at *2. T.C. did not have seizures within two days of vaccination, and the medical records do not document that she had status epilepticus after the vaccinations at issue here.

autoimmune disease in children. He cited an article by Bach to support this inference. Bach discussed the "hygiene hypothesis" and the implications related to allergic illnesses (e.g., asthma) and autoimmune diseases (e.g., multiple sclerosis). Pet. Ex. 80 at 7. Generally, Bach described the relationship between "the reduction in the incidence of infectious disease and the increase in the incidence of allergic and autoimmune diseases," and recommended research to more fully explore the nature and mechanisms that may play a role in these relationships. Id. at 8. Bach emphasized, however, that '[i]t is important to stress that there are no solid data indicating either a positive or negative role of vaccinations in the development of autoimmune or allergic diseases." Id. Further, the article does not touch on the subject of seizure disorders or epilepsy, or any association between vaccinations and these illnesses. It is not clear why Dr. Levin cited Bach, or how it supports his mechanistic theory.

Several other opinions or statements were made by Dr. Levin that were similarly conclusory or irrelevant and unsupported by medical literature or other evidence. For example, he opines that vaccines stimulate the immune system which "disrupts the homeostatic balance of the immune system" and "causes most of the vaccine adverse events." Pet. Ex. 15 at 4. He did not, however, describe how vaccines disrupt the homeostatic balance of the immune system, explain the statement, or how it relates to his theory, nor did he provide supportive medical literature on this point.

In summary, petitioner has not provided a sound and reliable theory to explain how the vaccinations at issue, given the facts and circumstances, can cause a seizure disorder, epilepsy, and T.C.'s other neurological problems. The undersigned has previously found that vaccination can cause the release of proinflammatory cytokines, and that vaccine-associated proinflammatory cytokines may cause complex febrile seizures which can trigger epilepsy if they occur within a medically reasonably temporal interval. See Ginn ex rel. R.G. v. Sec'y of Health & Hum. Servs., No. 16-1466V, 2021 WL 1558342 (Fed. Cl. Spec. Mstr. Mar. 26, 2021); Fuller ex rel. B.F. v. Sec'y of Health & Hum. Servs., No. 15-1470V, 2019 WL 7576382 (Fed. Cl. Spec. Mstr. Dec. 17, 2019). Here, however, T.C.'s onset did not occur within a medically reasonable temporal interval following her vaccinations, as discussed below. Additionally, the injured parties in Ginn and Fuller had febrile seizures, whereas, here, T.C. had afebrile seizures. Thus, the facts and circumstances of this case do not support vaccine causation. For all of the reasons discussed above, the undersigned finds that petitioner has failed to provide a sound and reliable theory, given the facts and circumstances of this particular case, that proinflammatory cytokines caused T.C.'s seizure disorder, epilepsy, and other neurological conditions.

2. Althen Prong Two

Under Althen Prong Two, petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d

at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

Since petitioner failed to prove Althen Prong One, it follows that she cannot prove Althen Prong Two. However, even if petitioner had proven a sound and reliable causal mechanism, she failed to prove by preponderant evidence a logical sequence of cause and effect, showing that T.C.'s vaccinations caused T.C.'s condition for three reasons: T.C.'s clinical course is not consistent with vaccine-related seizures, epilepsy, and epileptic encephalopathy; the treating physicians did not associate her condition with her vaccinations; and there are potential alternative causes for her disorder.

T.C.'s clinical course is not consistent with vaccine causation for several reasons. First, she had a progression of symptoms that began as exaggerated reflexes (Dr. Levin's opinion) and/or "benign myoclonic jerks" (treating physician, Dr. Duchatelier's opinion) which had occurred since her birth on September 9, 2013. On December 14, 2013, T.C. first had exotropia as described by T.C.'s treating doctor, Dr. Ferrand. Dr. Ferrand did not attribute this finding to T.C.'s vaccinations, and it was not observed nor documented until approximately one month after her two month vaccinations administered on November 13, 2013.[51]

T.C.'s next abnormal neurological findings were inability to fixate on objects properly and head lag, noted by Dr. Ferrand on January 29, 2014. These symptoms occurred in the context of an upper respiratory infection, three days after documented fever (temperature 100.3) and nasal congestion. These symptoms occurred sixteen days after T.C.'s four month vaccinations. Dr. Ferrand did not attribute these abnormalities to T.C.'s vaccinations.

The first clear evidence of seizure as documented by health care providers occurred on January 30, 2014, when T.C. had loud sounds when feeding and her body tensed up like she could not breath for about one minute. She was evaluated at Good Samaritan ED, where Dr. Badleo observed that T.C. was constantly thrashing around and unable to make eye contact. T.C. was assessed with possible febrile seizure. The next day, January 31, T.C. was evaluated by Dr. Shah who documented the history of upper respiratory symptoms four days prior to the episode which brought T.C. to the hospital. An EEG showed abnormalities consistent with epileptic activity. T.C.'s MRIs were normal, and did not show any evidence of disruption of the blood brain barrier or inflammation to support Dr. Levin's theory of based on proinflammatory cytokines.

[51] T.C. received her two month vaccinations on November 13, 2013, and the first notation of exotropia in her medical records was dated on December 14, 2013. Pet. Ex. 2 at 39.

The physicians who saw T.C. in the hospital after she presented on January 30, were impressed with and noted her history of movements (exaggerated startle or twitches) since birth. They also noted her history of an abnormal eye examination and head lag. In summary, as described by Dr. Wiznitzer, the records illustrate a progression of symptoms over time, and this clinical course, along with the abnormal EEG, resulted in a diagnosis of epilepsy.

Given the theory proposed by Dr. Levin,[52] cytokines would be elevated for three to four days after each vaccination. Dr. Wiznitzer opined, however, that the records do not describe any significant worsening of T.C.'s condition in the days following any of her vaccinations. The undersigned finds Dr. Wiznitzer's opinion on this point more persuasive, as it is consistent with the chronology set forth in the contemporaneous medical records created by T.C.'s treating physicians.

Further, T.C.'s treating physicians did not attribute her epilepsy or encephalopathy to her vaccinations. On January 29, 2014, when T.C. was unable to fixate on objects and had head lag, Dr. Ferrand did not document any association with her vaccinations. On January 30, Dr. Badleo noted that T.C. was constantly thrashing around and did not make eye contact but did not relate the findings or potential seizure disorder to her vaccinations. On January 31, T.C. was seen by Dr. Shah and Dr. Duchatelier. Neither attributed the neurological findings or abnormal EEG showing epileptic activity to vaccinations. A review of the records fails to demonstrate that T.C.'s physicians attributed her seizures or epilepsy to her vaccinations.

Moreover, T.C.'s clinical deterioration occurred on January 30, 2014, when she had a seizure that occurred in the context of an upper respiratory infection. Dr. Wiznitzer opined that illness can provoke seizure activity. This raises the question of an alternative cause—that the upper respiratory infection may have been a trigger for the seizure and clinical deterioration. There is support for this position in the medical records. See Pet. Ex. 5 at 7 (noting T.C.'s diagnosis of nasal congestion and upper respiratory infection by Dr. Santangelo); Pet. Ex. 5 at 60 (documenting T.C.'s history of upper respiratory symptoms for four days prior and an episode of "stiffening of body with staring" from Dr. Shah).

The undersigned is not persuaded by petitioner's arguments, given T.C.'s clinical course, treating physicians' statements, the experts' opinions, and medical literature. The undersigned acknowledges that petitioner is not required to eliminate other potential causes in order to be entitled to compensation. See Walther v. Sec'y of Health & Hum. Servs., 485 F.3d 1146, 1149-52 (Fed. Cir. 2007) (finding petitioner does not bear the burden of eliminating alternative independent potential causes). However, she finds it reasonable to consider "evidence of other possible sources of injury"—here, T.C.'s upper respiratory infection—in determining "whether a

[52] Dr. Levin testified that the innate immune response is almost immediate, causing the production of proinflammatory cytokines within hours, while the adaptive immune response takes a week and lasts about a month, although it is not very serious after the first three to four days. Pet. Ex. 15 at 4. Dr. Levin opined that the adaptive immune T and B cells also produced cytokines. Id. This aspect of his opinion, however, was not well developed, and does not provide support for his theory.

prima facie showing has been made that the vaccine[s] [were] a substantial factor in causing the injury in question." Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine was a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

In addition to the issue of the upper respiratory infection, and its role in triggering the initial clinically notable seizure, there is the question about the role that T.C.'s genetic variant (GABRB2 de novo mutation) played in causing her seizures, epilepsy, and epileptic encephalopathy. There is support in the medical records to establish that T.C.'s physicians place significant weight on her GABRB2 genetic abnormality, and its role in her condition. For example, T.C.'s neurologist, Dr. Sykho, T.C.'s pediatrician, Dr. Jan, and Northwell Health Hospital Nurse Practitioner, Cristina Farrell, noted T.C.'s genetic abnormality in context with her illness. Resp. Ex. GG at 19; Resp. Ex. FF at 12; Pet. Ex. 37 at 3.

Dr. Wiznitzer devotes considerable time on this aspect of his opinion, and explains why he believed T.C.'s genetic variant is the cause of her epilepsy and encephalopathy. The genetic testing done at Columbia University Medical Center, however, stated that T.C.'s GABRB2 abnormality is of "uncertain clinical significance." Pet. Ex. 52 at 2. This phrase was repeated in March 2021, by Dr. Sykho, who noted that T.C. had genetic testing that revealed a variant of unknown significance in the GABRB2 gene. Dr. Sykho did not opine, however, that T.C.'s illness was solely due to her genetic abnormality. Thus, the testing and treating physician opinion evidence suggests that while T.C.'s genetic abnormality may be significant, there has been no identical mutation reported, and it remains of unknown significance. While the genetic abnormality may be the sole cause of T.C. condition, there is insufficient evidence for the undersigned to reach this conclusion at this time. It is reasonable, however, to consider "evidence of other possible sources of injury"—T.C.'s genetic abnormality—in determining "whether a prima facie showing has been made that the vaccine[s] [were] a substantial factor in causing the injury in question." Stone, 676 F.3d at 1379.

Evidence of other sources of injury, here, T.C.'s upper respiratory infection and her genetic abnormality, are "relevant not only to the 'factors unrelated' defense, but also to whether a prima facie showing has been made that the vaccine[s] [were] a substantial factor in causing the injury in question." Stone, 676 F.3d at 1379; see also de Bazan, 539 F.3d at 1353 ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations."). But see Sharpe v. Sec'y of Health & Hum. Servs., 964

F.3d 1072, 1082 (Fed. Cir. 2020) (finding there was no substantial evidence to support that the vaccinee's genetic mutation was more likely than not the sole, substantial factor causing her severe seizure disorder).

For all of the reasons described above, the undersigned finds that petitioner has failed to provide preponderant evidence of a logical sequence of cause and effect required under Althen Prong Two.

3. Althen Prong Three

Althen Prong Three requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542.

Both experts place the initial onset of T.C.'s seizure disorder which lead to her epilepsy on the date that she began having "enhanced startle reflexes" or "twitches," although they disagree as to the date that these abnormalities began.

Dr. Levin offered three opinions as to onset. In an expert report, he opined that T.C.'s initial neurological abnormality was her "enhanced startle reflex at one month of age," followed by twitches of her left arm, which progressed to a seizure disorder. Pet. Ex. 15 at 3. At the hearing, Dr. Levin testified that T.C.'s enhanced startle reflexes began after vaccination, and that T.C. received her first vaccination, a hepatitis B vaccine, on day one or two after birth. Tr. 50, 52. However, he also testified that T.C. had seizures within five days of vaccination, on October 9, 2013,[53] when her mother noted an exaggerated startle reflex, which Dr. Levin opined was, in hindsight, the beginning of T.C.'s seizure disorder. Tr. 99. Thus, Dr. Levin's opinions are internally inconsistent.

In addition to being internally inconsistent, there are additional problems with Dr. Levin's opinions as to onset. The most contemporaneous medical records by three different physicians establish that T.C.'s twitches, or enhanced startle reflexes, were present "since birth," and did not begin at one month of age. On January 30, 2014, T.C. was evaluated by Dr. Badleo, when she was brought to Good Samaritan after she had an event described as "body tensed up like she couldn't breath[e] for about 1 min[ute]." Pet. Ex. 5 at 31-32. Dr. Badleo took a history from petitioner, who reported that T.C. had constant twitches since birth, which "as per mom, she was born [with]." Id. at 33. The next day, January 31, T.C. was seen by Dr. Shah, who documented that "[p]arents state [T.C. had] intermittent 'shivering' movements since birth." Id.

[53] Although Dr. Levin testified that October 9 was within five days of vaccination, he was incorrect. T.C. did not receive any vaccinations within five days of October 9, 2013.

at 60. On that same day, T.C. was also evaluated by Dr. Duchatelier, who wrote, "Mom had [] concerns about what sounds like benign myoclonic jerks (1 or 2 at a time) of mostly left shoulder that have occurred off and on since birth." Id. at 69. Thus, three independent physicians all documented a consistent history reported by the parents that the abnormal movements at issue had occurred since birth.

T.C.'s pediatrician did not note the "startle" or "twitches" in his early records. According to petitioner's affidavit, petitioner told the pediatrician T.C. had twitches since birth and that at one month old T.C. startled for no reason. Dr. Ferrand told petitioner the twitches and startle movements were normal and were just due to her immature nervous system. Petitioner's testimony, that Dr. Ferrand dismissed her concerns because the movements were thought to be normal, explains why the pediatrician's early records do not include references to the twitching and startle movements. Taken together, petitioner's statements, the pediatricians records, and the later records are all consistent. Only later testimony from petitioner, that the twitching and shivering movements did not occur until one month, is inconsistent, and thus, less reliable. Moreover, the weight of the evidence establishes that the twitches were present since birth.

Medical records, "in general, warrant consideration as trustworthy evidence." Cucuras, 993 F.2d at 1528. Accordingly, where subsequent testimony conflicts with contemporaneous medical records, special masters usually accord more weight to the medical records. See, e.g., Reusser v. Sec'y of Health & Hum. Servs., 28 Fed. Cl. 516, 523 (1993) ("[W]ritten documentation recorded by a disinterested person at or soon after the event at issue is generally more reliable than the recollection of a party to a lawsuit many years later."); Rogero v. Sec'y of Health & Hum. Servs., No. 11-770V, 2017 WL 4277580, at *37 (Fed. Cl. Spec. Mstr. Sept. 1, 2017), aff'd, 748 F. App'x 996 (Fed. Cir. 2018). Additionally, special masters under the Vaccine Act have in most cases declined to credit later testimony over contemporaneous records. See, e.g., Stevens v. Sec'y of Health & Hum. Servs., No. 90-221V, 1990 WL 608693, at *3 (Fed. Cl. Spec. Mstr. Dec. 21, 1990); see also Vergara v. Sec'y of Health & Hum. Servs., No. 08-882V, 2014 WL 2795491, at *4 (Fed. Cl. Spec. Mstr. May 15, 2014) ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those recorded in later medical histories, affidavits, or trial testimony."); Cucuras, 993 F.2d at 1528 (noting that "the Supreme Court counsels that oral testimony in conflict with contemporaneous documentary evidence deserves little weight").

The next problem is that some of Dr. Levin's opinions as to onset were based on factually incorrect information. At the hearing, Dr. Levin initially placed the date of T.C.'s first vaccination at day one or two after birth, (Tr. 54) while the medical records document that T.C. did not receive her first vaccine until day four, September 13, when she presented to her pediatrician's office. He also opines that T.C.'s startle reflex began on October 9, which he testified was within five days of vaccination. See Tr. 99. October 9, however, was three weeks after T.C.'s first hepatitis B vaccination, not five days post-vaccination. The undersigned finds the opinions of Dr. Levin based on inaccurate foundational evidence to be unsupported and unreliable.

In contrast, Dr. Wiznitzer based his opinion on the contemporaneous medical records which place the onset of T.C.'s enhanced startle reflexes or twitches as occurring since birth.

Resp. Ex. A at 12. Dr. Wiznitzer opined that T.C.'s twitches, noted from birth, were evidence of her epilepsy disorder. Although Dr. Wiznitzer opined that T.C. was born with her condition, he persuasively explained that after the initial manifestations begin, T.C.'s condition evolved over time. Id. Here, T.C. had abnormal movements, twitching, abnormal eye movements, and feeding issues, and then the seizure manifestations of epilepsy began. Tr. 170.

Based on the contemporaneous records by the treating physicians, as described above, the undersigned finds that T.C.'s abnormal movements, twitches, or enhanced startle reflexes occurred since birth. Specifically, as to the onset of T.C.'s encephalopathy, both Dr. Levin and Dr. Wiznitzer agree. Dr. Levin opined that T.C.'s CNS disorder began in December 2013, when T.C.'s pediatrician noted exotropia. Dr. Wiznitzer agreed and opined that T.C.'s encephalopathy manifested when she had exotropia, documented on December 14, 2013.

Further, based on the opinions of Dr. Wiznitzer, as well as the contemporaneous medical records, and all of the evidence filed in this matter, the undersigned finds that T.C. was born with her condition, and that her condition was first manifested by her abnormal movements, referred to as enhanced startle reflexes or twitches. The undesigned finds exotropia to be the initial manifestation of her encephalopathy. T.C.'s clinical deterioration and clinically documented seizures, all well-documented by her treating physicians from January 26 to 30, 2014, were also manifestations of her epileptic encephalopathy.[54]

Based on a review of all of the evidence, the undersigned finds that petitioner has failed to prove by preponderant evidence that an onset of symptoms after vaccination occurred in an appropriate time frame of three to four days after vaccination. Therefore, petitioner has failed to provide preponderant evidence to satisfy Althen Prong Three.

VII. CONCLUSION

It is clear that petitioner has had a very difficult struggle caring for T.C. since shortly after her birth, and the undersigned extends her sympathy to petitioner and to T.C. for the overwhelming issues that they have faced. The undersigned's decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

For all of the reasons discussed above, the undersigned finds that petitioner has not established by preponderant evidence that vaccination caused T.C.'s condition. Therefore, petitioner is not entitled to compensation and the petition must be dismissed. In the absence of a timely filed motion for review pursuant to Vaccine Rule 23, the Clerk of Court **SHALL ENTER JUDGMENT** in accordance with this Decision.

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[54] While the treating physicians noted her history of exotropia, it does not appear that they diagnosed T.C. with epileptic encephalopathy based on that finding. The diagnosis of epileptic encephalopathy was documented in May 2014, after T.C. was hospitalized due to her clinical deterioration. Pet. Ex. 8 at 497, 506. Regardless of whether T.C.'s onset of epileptic encephalopathy manifested as early as December 14, 2013, when she had exotropia, or later in May 2014, when the diagnosis of epileptic encephalopathy was documented, the undersigned does not find there to be any temporal association with T.C.'s vaccinations.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master